Supplemental Methods

Chemical Synthesis

General. Solvents and liquid reagents were dried according to standard procedures: THF and toluene were distilled over Na and benzophenone, CH_2Cl_2 from P_2O_5, and MeOH, DMF, Et_3N, and pyridine from CaH_2. Technical solvents were distilled: EtOAc, $CHCl_3$, and CH_2Cl_2 over K_2CO_3; cyclohexane, hexane, MeOH, and toluene without any additive. Anal. TLC: precoated silica gel plates (*Merck* silica gel *60 F*254); detection by heating with 'mostain' (400 mL of 10% H_2SO_4 soln., 20 g of $(NH_4)_6Mo_7O_{24}\cdot 6\ H_2O$, 0.4 g of $Ce(SO_4)_2$). Flash chromatography (FC): silica gel *Merck* under slightly elevated pressure (0.15–0.3 bar of N_2) using distilled technical solvents as eluent. Melting points (m.p.) were measured on *Büchi B-545* in open capillaries. Optical rotations: 1–dm cell at 589 nm (25°C). IR spectra (*Perkin-Elmer 1600 FT-IR* spectrometer): neat (ATR); absorption in cm^{-1}; intensities given as *s* (strong), *m* (medium), and *w* (weak). NMR spectra were recorded at 23–26 °C; chemical shifts (δ) in ppm (relative to TMS) and coupling constants (*J*) in Hz. Multiplicities of signals: *s* (singlet), *d* (doublet), *t* (triplet), *q* (quartet), and *m* (multiplet). The assignment of the ^{1}H- and ^{13}C-NMR signals of all products is based on DQF-COSY, TOCSY, HSQC, and HMBC spectra, individual couplings and couplings for signals carrying an asterisk (*) could not determined due to signal overlap. HR-MALDI-MS recorded with gentisic acid (= 2,4-dihydroxybenzoic acid, DHB) as matrix. "Processing as usual": extraction with the solvent indicated, washing of the org. phase with brine, drying with $MgSO_4$ or Na_2SO_4, and evaporation of the filtrate under reduced pressure.

General Procedure for O-Alkylation of **2** (GP 1). NaH (60% dispersion in oil; 1.5 eq.) was added to a soln. of **2** (2) (1 eq.) in dry DMF (0.1 M) at 0 °C. The mixture was stirred until H_2 evolution ceased, and then treated dropwise with the alkyl halide (1.5 eq.) followed by addition of TBAI (0.1 eq.) in one portion. The mixture was stirred at 26 °C for 6–24 h, treated with

crushed ice, and extracted with EtOAc (3 x). The combined organic phases were washed with water and brine, dried over $MgSO_4$, filtered, and evaporated. FC gave the alkyl ethers.

General Procedure for the Deprotection and Reduction of Azido 4-Methoxybenzyl (PMB) *Ethers* (GP 2). A 0.01 M soln. of the azido PMB ether (1 eq.) in CH_3CN/H_2O 9:1 was treated with ceric ammonium nitrate (CAN; 8 eq.), and stirred at 26 °C for 5 h. The mixture was cooled to 0 °C, treated with a 1 N aq. soln. of $NaBH_4$ (10 eq.), and extracted with EtOAc (3 x). The combined organic phases were washed with brine, dried ($MgSO_4$), and evaporated. A 0.03 M soln. of the resulting azido alcohol (1 eq.) in THF was treated with 0.1 N NaOH (1.5 eq.) and 1 M PMe_3 in THF (6 eq.), stirred at 60 °C for 4–8 h, and evaporated. FC of the residue gave the deprotected 4-*O*-alkylparomomycin.

1,3,2',2''',6'''-Pentazido-1,3,2',2''',6'''-pentadeamino-6,3',2'',5'',3''',4'''-hexakis-O-*(4-methoxybenzyl)-4'*-O-*methyl-6'*-O-*(monomethoxytrityl)paromomycin* (**3**). Alkylation of 300 mg **2** with 16.1 µL MeI according to GP 1 and FC (pentane/EtOAc 7:3) gave **3** (205 mg, 68%) as a colorless oil. R_f (pentane/EtOAc 7:3) 0.45. IR (ATR): 2934*w*, 2836*w*, 2100*s*, 1611*m*, 1586*w*, 1512*s*, 1463*w*, 1359*w*, 1301*w*, 1245*s*, 1174*m*, 1110*m*, 1070*m*, 1033*s*. ^{1}H-NMR (600 MHz, $CDCl_3$): 7.59–6.59 (*m*, 38 arom. H); 6.29 (*d*, *J* = 3.6, H–C(1')); 5.70 (*d*, *J* = 6.3, H–C(1'')); 4.93 (*d*, *J* = 10.2, ArC*H*); 4.89 (*d*, *J* = 1.8, H–C(1''')); 4.77 (br. *s*, ArCH_2); 4.61 (*d*, *J* = 10.3, ArC*H*); 4.58 (*d*, *J* = 11.0, ArC*H*); 4.56 (*d*, *J* = 11.1, ArC*H*); 4.53 (*d*, *J* = 11.1, ArC*H*); 4.45 (*d*, *J* = 10.8, ArC*H*); 4.42 (*d*, *J* = 11.0 , ArC*H*); 4.35 (*d*, *J* = 11.4, ArC*H*); 4.31 (*d*, *J* = 11.8, ArC*H*); 4.29 (*q*, *J* ≈ 2.4, H–C(4'')); 4.22–4.20 (*m*, H–C(3'')); 4.19 (*d*, *J* = 10.4, ArC*H*); 4.09 (*ddd*, *J* = 10.0, 4.9, 1.8, H–C(5')); 4.00–3.97 (*m*, H–C(5), H–C(3'), H–C(2'')); 3.82–3.81 (*m*, H–C(4), H_a–C(5'')); 3.81 (*s*, 2 OMe); 3.80, 3.79, 3.78, 3.76 (4*s*, 4 OMe); 3.74–3.72 (*m*, H–C(3''')); 3.66 (*s*, OMe); 3.66–3.62 (*m*, H_a–C(6''')); 3.56 (*dd*, *J* = 10.2, 3.1, H_b–C(5'')); 3.51–3.46 (*m*, H–C(3)); 3.45–3.38 (*m*, H–C(1), H_a–C(6')); 3.40–3.39 (*m*, H–C(2''')); 3.32–3.28 (*m*, H–C(6), H–C(4')); 3.31 (*s*, MeO–C4')); 3.17 (*dd*, *J* = 10.3, 3.6, H–C(2')); 3.15 (*dd*, *J* = 10.0, 5.1, H_a–C(6')); 3.07 (br. *s*,

H–C(4’’’)); 2.82 (*dd*, *J* = 12.9, 4.0, H_b–C(6’’’)); 2.22 (*dt*, *J* = 13.1, 4.5, H_{eq}–C(2)); 1.37 (*q*, *J* = 12.9, H_{ax}–C(2)). ^{13}C-NMR (150 MHz, $CDCl_3$): 159.8, 159.7, 159.5, 159.3, 159.2, 159.0, 158.7 (7*s*, 7 C_{Ar}–OMe); 145.0, 144.6, 135.9 (3*s*, 3 C(1) of MMTr); 130.6–126.9 (several *d* and *s*); 114.1–113.2 (several *d*) (6 C(1) of PMB, CH’s of PMB and MMTr); 106.0 (*d*, C(1’’)); 98.8 (*d*, C(1’’’)); 95.7 (*d*, C(1’)); 86.1 (*s*, CAr_3); 84.2 (*d*, C(6)); 83.0 (*d*, C(5)); 82.3 (*d*, C(4’’)); 82.0 (*d*, C(2’’)); 80.9 (*d*, C(4’)); 80.0 (*d*, C(3’)); 75.8 (*d*, C(3’’)); 75.3, 74.9 (2*t*, 2 ArCH_2); 74.5 (*d*, C(5’’’)); 74.4 (*d*, C(4)); 73.5, 73.2 (2*t*, 2 ArCH_2); 72.7 (*d*, C(3’’’)); 72.1 (*t*, ArCH_2); 71.4 (*d* and *t*, C(5’), ArCH_2); 71.3 (*d*, C(4’’’)); 70.2 (*t*, C(5’’)); 63.5 (*d*, C(2’)); 62.9 (*t*, C(6’)); 60.8 (*q*, MeO–C(4’)); 60.6 (*d*, C(1)); 60.3 (*d*, C(3)); 57.5 (*d*, C(2’’’)); 55.4 (*q*, 3 OMe); 55.3 (*q*, 2 OMe); 55.2, 54.8 (2*q*, 2 OMe); 51.2 (*t*, C(6’’’)); 32.9 (*t*, C(2)). HR-MALDI-MS: 1774.7188 (90, $[M + Na]^+$, $C_{92}H_{101}N_{15}NaO_{21}^+$; calc. 1774.7189).

1,3,2’,2’’’,6’’’-Pentazido-1,3,2’,2’’’,6’’’-pentadeamino-6,3’,2’’,5’’,3’’’,4’’’-hexakis-O-*(4-methoxybenzyl)-4’*-O-*ethyl-6’*-O-*(monomethoxytrityl)paromomycin* (**4**). Alkylation of 1.90 g of **2** with 0.12 mL of EtBr according to GP 1 and FC (pentane/EtOAc 7:3) gave **4** (1.70 g, 88%) as colorless viscous oil. R_f (pentane/EtOAc 7:3) 0.46. $[\alpha]_D^{23}$ = +53.0 (*c* = 0.6, $CHCl_3$). IR (ATR): 2933*w*, 2837*w*, 2100*s*, 1611*m*, 1585*w*, 1512*s*, 1463*w*, 1359*w*, 1301*w*, 1246*s*, 1174*m*, 1110*m*, 1070*m*, 1033*s*. ^{1}H-NMR (600 MHz, $CDCl_3$): 7.58–6.59 (*m*, 38 arom. H); 6.27 (*d*, *J* = 3.7, H–C(1’)); 5.70 (*d*, *J* = 6.3, H–C(1’’)); 4.93 (*d*, *J* = 10.3, ArC*H*); 4.89 (*d*, *J* = 1.8, H–C(1’’’)); 4.74 and 4.72 (2*d*, *J* = 10.3, ArCH_2); 4.61 (*d*, *J* = 10.3, ArC*H*); 4.57 (*d*, *J* = 11.1, ArC*H*); 4.55 (*d*, *J* = 11.1, ArC*H*); 4.53 (*d*, *J* = 10.3, ArC*H*); 4.45 (*d*, *J* = 11.6, ArC*H*); 4.42 (*d*, *J* = 11.6, ArC*H*); 4.35 (*d*, *J* = 11.4, ArC*H*); 4.31 (*d*, *J* = 11.4, ArC*H*); 4.30–4.28 (*m*, H–C(4’’)); 4.22–4.20 (*m*, H–C(3’’)); 4.20 (*d*, *J* = 10.3, ArC*H*); 4.09 (*ddd*, *J* = 10.0, 5.1, 1.4, H–C(5’)); 4.00–3.96 (*m*, H–C(5), H–C(3’), H–C(2’’)); 3.83 (*dd*, *J* = 9.4, 9.8, H–C(4)); 3.82–3.81 (*m*, H_a–C(5’’), OMe); 3.81, 3.80, 3.79, 3.78, 3.75 (5*s*, 5 OMe); 3.74–3.72 (*m*, H–C(3’’’), H–C(5’’’)); 3.67–3.65 (*m*, OCH_aMe); 3.61 (*dd*, *J* = 13.0, 8.3, H_a–C(6’’’)); 3.56 (*dd*, *J* = 10.3, 3.0, H_b–C(5’’)); 3.49 (*ddd*, *J* = 12.7, 9.8, 4.7, H–C(3)); 3.46–3.41 (*m*, H–C(1), H_a–C(6’)); 3.40–3.39 (*m*, H–C(2’’’)); 3.36–3.30 (*m*, H–

C(6), H–C(4'), O*CH*$_b$Me); 3.17 (*dd*, *J* = 10.4, 3.7, H–C(2')); 3.13 (*dd*, *J* = 10.0, 5.1, H$_b$–C(6')); 3.07 (br. *s*, H–C(4''')); 2.82 (*dd*, *J* = 13.0, 4.0, H$_b$–C(6''')); 2.23 (*dt*, *J* = 13.1, 4.7, H$_{eq}$–C(2)); 1.39 (*q*, *J* = 12.7, H$_{ax}$–C(2)); 0.91 (*t*, *J* = 7.1, OCH$_2$*Me*). ^{13}C-NMR (150 MHz, $CDCl_3$): 159.8, 159.7, 159.5, 159.4, 159.2, 159.0, 158.7 (7*s*, 7 *C*$_{Ar}$–OMe); 144.9, 144.6, 136.0 (3*s*, 3 C(1) of MMTr); 130.6–127.0 (several *d* and *s*) and 114.2–113.2 (several *d*) (6 C(1) of PMB, CH's of PMB and MMTr); 106.0 (*d*, C(1'')); 98.8 (*d*, C(1''')); 95.7 (*d*, C(1')); 86.1 (*s*, *C*Ar$_3$); 84.2 (*d*, C(6)); 83.0 (*d*, C(5)); 82.3 (*d*, C(4'')); 82.0 (*d*, C(2'')); 80.0 (*d*, C(3')); 78.9 (*d*, C(4')); 75.8 (*d*, C(3'')); 75.3, 74.9, 74.5 (3*t*, 3 Ar*C*H$_2$); 74.5 (*d*, C(5''')); 74.4 (*d*, C(4)); 73.5, 73.2 (2*t*, 2 Ar*C*H$_2$); 72.7 (*d*, C(3''')); 71.5 (*d*, C(5')); 71.4 (*t*, Ar*C*H$_2$); 71.2 (*d*, C(4''')); 70.2 (*t*, C(5'')); 68.2 (*t*, O*C*H$_2$Me); 63.6 (*d*, C(2')); 62.9 (*t*, C(6')); 60.6 (*d*, C(1)); 60.2 (*d*, C(3)); 57.5 (*d*, C(2''')); 55.4 (*q*, 3 OMe); 55.3 (*q*, 3 OMe); 54.8 (*q*, OMe); 51.2 (*t*, C(6''')); 32.9 (*t*, C(2)); 15.7 (*q*, OCH$_2$*Me*). HR-MALDI-MS: 1789.7376 (100, $[M + Na]^+$, $C_{93}H_{103}N_{15}NaO_{21}^+$; calc. 1789.8900).

1,3,2',2''',6'''-Pentazido-1,3,2',2''',6'''-pentadeamino-6,3',2'',5'',3''',4'''-hexakis-O-*(4-methoxybenzyl)-4'*-O-*propyl-6'*-O-*(monomethoxytrityl)paromomycin* (**5**). Alkylation of 530 mg of **2** with 27.8 μL 1-bromopropane according to GP 1 and FC (pentane/EtOAc 7:3) gave **5** (430 mg, 79%) as a colorless viscous oil. R_f (pentane/EtOAc 7:3) 0.36. $[\alpha]_D^{23}$ = +54.5 (*c* = 0.3, $CHCl_3$). IR (ATR): 2934*w*, 2838*w*, 2100*s*, 1611*m*, 1585*w*, 1512*s*, 1463*w*, 1302*w*, 1246*s*, 1174*m*, 1108*m*, 1060*m*, 1033*s*. ^{1}H-NMR (600 MHz, $CDCl_3$): 7.58–6.58 (*m*, 38 arom. H); 6.28 (*d*, *J* = 3.6, H–C(1')); 5.70 (*d*, *J* = 6.2, H–C(1'')); 4.93 (*d*, *J* = 10.1, ArC*H*); 4.89 (*d*, *J* = 1.8, H–C(1''')); 4.75 and 4.73 (2*d*, *J* = 10.3, ArC*H*$_2$); 4.60 (*d*, *J* = 10.1, ArC*H*); 4.57 (*d*, *J* = 11.3, ArC*H*); 4.55 (*d*, *J* = 11.8, ArC*H*); 4.52 (*d*, *J* = 11.3, ArC*H*); 4.45 (*d*, *J* = 11.3, ArC*H*); 4.42 (*d*, *J* = 11.8, ArC*H*); 4.34 (*d*, *J* = 11.3, ArC*H*); 4.30 (*d*, *J* = 11.8, ArC*H*); 4.28 (*q*, *J* ≈ 2.4, H–C(4'')); 4.21 (*dd*, *J* = 4.9, 2.2, H–C(3'')); 4.19 (*d*, *J* = 11.8, ArC*H*); 4.11 (*ddd*, *J* = 10.1, 5.0, 1.5, H–C(5')); 4.00–3.97 (*m*, H–C(5), H–C(3'), H–C(2'')); 3.85 (*dd*, *J* = 9.1, 9.8, H–C(4)); 3.81 (s, OMe); 3.81–3.80 (m, H$_a$–C(5''), OMe); 3.79, 3.77, 3.75 (3*s*, 3 OMe); 3.74–3.72 (*m*, H–C(3'''), H–C(5''')); 3.66 (*s*, OMe); 3.61 (*dd*, *J* = 13.1, 8.6, H$_a$–C(6''')); 3.60–3.57 (*m*, O*CH*$_a$CH$_2$Me); 3.56 (*dd*, *J* = 10.3, 2.9,

H_b–C(5’’)); 3.49 (*ddd*, *J* = 12.4, 9.8, 4.6, H–C(3)); 3.46–3.44 (*m*, H_a–C(6’)); 3.42 (*ddd*, *J* = 12.4, 9.5, 4.6, H–C(1)); 3.40–3.39 (*m*, H–C(2’’’)); 3.34 (*s*, OMe); 3.33–3.30 (*m*, H–C(6), H–C(4’)); 3.20–3.16 (*m*, H–C(2’), O*CH*$_b$CH$_2$Me); 3.13 (*dd*, *J* = 10.2, 5.0, H_b–C(6’)); 3.07 (br. *s*, H–C(4’’’)); 2.82 (*dd*, *J* = 13.1, 4.1, H_b–C(6’’’)); 2.23 *(dt*, *J* = 13.1, 4.6, H_{eq}–C(2)); 1.39 (*q*, *J* = 12.4, H_{ax}–C(2)); 1.32–1.26 (*m*, OCH$_2$*CH*$_2$Me); 0.66 (*t*, *J* = 7.1, O(CH$_2$)$_2$*Me*). ^{13}C-NMR (150 MHZ, $CDCl_3$): 159.8, 159.7, 159.5, 159.4, 159.2, 159.0, 158.7 (7s, 7 C_{Ar}–OMe); 144.9, 144.6, 136.0 (3*s*, 3 C(1) of MMTr); 130.6–126.9 (several *d* and *s*) and 114.3–113.2 (several *d*) (6 C(1) of PMB, CH’s of PMB and MMTr); 106.0 (*d*, C(1’’)); 98.9 (*d*, C(1’’’)); 95.7 (*d*, C(1’)); 86.1 (*s*, *C*Ar$_3$); 84.1 (*d*, C(6)); 83.0 (*d*, C(5)); 82.4 (*d*, C(4’’)); 82.1 (*d*, C(2’’)); 80.0 (*d*, C(3’)); 79.0 (*d*, C(4’)); 75.8 (*d*, C(3’’)); 75.3, 74.9 (2*t*, 2 ArCH$_2$); 74.4 (*d*, C(5’’’)); 74.3 (*d*, C(4)); 73.5, 73.3 (2*t*, 2 Ar*C*H$_2$); 72.9 (*t*, O*CH*$_2$CH$_2$Me); 72.7 (*d*, C(3’’’)); 72.1 (*t*, Ar*C*H$_2$); 71.6 (*d*, C(5’)); 71.4 (*t*, Ar*C*H$_2$); 71.2 (*d*, C(4’’’)); 70.2 (*t*, C(5’’)); 63.6 (*d*, C(2’)); 63.0 (*t*, C(6’)); 60.6 (*d*, C(1)); 60.3 (*d*, C(3)); 57.5 (*d*, C(2’’’), 55.4, 55.4, 55.3, 55.3, 54.9 (*q*, OMe); 51.2 (*t*, C(6’’’)); 32.9 (*t*, C(2)); 23.5 (*t*, OCH$_2$*CH*$_2$CH$_3$); 10.5 (*q*, CH$_3$). HR-MALDI-MS: 1803.7532 (100, [*M* + Na]$^+$, $C_{94}H_{105}N_{15}NaO_{21}^+$; calc. 1803.7541).

1,3,2’,2’’’,6’’’-Pentazido-1,3,2’,2’’’,6’’’-pentadeamino-6,3’,2’’,5’’,3’’’,4’’’-hexakis-O-*(4-methoxybenzyl)-4’*-O-*butyl-6’*-O-*(monomethoxytrityl)paromomycin* (**6**). Alkylation of 724 mg of **2** with 67.7 µL of 1-bromobutane according to GP 1 and FC (hexane/ EtOAc 7:3) gave **6** (0.66 g, 86%) as a colorless viscous oil. R_f (hexane/EtOAc 7:3) 0.35. $[\alpha]_D^{23}$ = +48.7 *(c* = 0.5, $CHCl_3$). IR (ATR): 2934*w*, 2836*w*, 2100*s*, 1611*m*, 1585*w*, 1512*s*, 1464*w*, 1361*w*, 1301*w*, 1246*s*, 1173*m*, 1111*m*, 1071*m*, 1032*s*. ^{1}H-NMR (600 MHz, $CDCl_3$): 7.58–6.58 (*m*, 38 arom. H); 6.28 (*d*, *J* = 3.7, H–C(1’)); 5.70 (*d*, *J* = 6.3, H–C(1’’)); 4.93 (*d*, *J* = 10.2, ArC*H*); 4.90 (*d*, *J* = 1.8, H–C(1’’’)); 4.75 and 4.73 (2*d*, *J* = 10.3, ArC*H*$_2$); 4.61 (*d*, *J* = 10.2, ArC*H*); 4.57 (*d*, *J* = 11.2, ArC*H*); 4.58 (*d*, *J* = 11.9, ArC*H*); 4.52 (*d*, *J* = 11.2, ArC*H*); 4.46 (*d*, *J* = 11.2, ArC*H*); 4.41 (*d*, *J* = 11.9, ArC*H*); 4.35 (*d*, *J* = 11.2, ArC*H*); 4.31 (*d*, *J* = 11.8, ArC*H*); 4.29 (*q*, *J* ≈ 2.4, H–C(4’’)); 4.22–4.20 (*m*, H–C(3’’)); 4.20 (*d*, *J* = 11.8, ArC*H*); 4.12 (*ddd*, *J* = 10.1, 5.0, 1.8, H–C(5’)); 4.01–3.99 (*m*, H–

C(5)); 3.98 (*dd*, *J* = 6.3, 4.8, H–C(2'')); 3.98–3.96 (*m*, H–C(3')); 3.87 (*t*, *J* = 9.6, H–C(4)); 3.82–3.80 (*m*, H_a–C(5''), 2 OMe); 3.79, 3.78, 3.75 (3*s*, 3 OMe); 3.74–3.73 (*m*, H–C(5''')); 3.73 (*dd*, J = 3.4, 2.7, H–C(3''')); 3.66 (*s*, OMe); 3.66–3.60 (*m*, H_a–C(6'''), OC$H_a$$(CH_2)_2$Me); 3.56 (*dd*, *J* = 10.4, 2.9, H_b–C(5'')); 3.50 (*ddd*, *J* = 12.4, 9.6, 4.6, H–C(3)); 3.46–3.42 (*m*, H–C(1), H_a–C(6')); 3.40–3.39 (*m*, H–C(2''')); 3.36 (*s*, OMe); 3.32 (*t*, *J* = 9.4 H–C(6)); 3.29 (*t*, *J* = 9.4, H–C(4')); 3.23–3.20 (*m*, OC$H_b$$(CH_2)_2$Me); 3.15 (*dd*, *J* = 10.1, 5.0, H_b–C(6')); 3.14 (*dd*, *J* = 10.2, 3.7, H–C(2'); 3.07 (br. *s*, H–C(4''')); 2.82 (*dd*, *J* = 13.0, 4.0, H_b–C(6''')); 2.23 (*dt*, *J* = 13.1, 4.6, H_{eq}–C(2)); 1.40 (*q*, *J* = 12.4, H_{ax}–C(2)); 1.31–1.22 (*m*, $OCH_2CH_2CH_2$Me); 1.15–1.01 (*m*, $O(CH_2)_2CH_2$Me); 0.78 (*t*, *J* = 7.4, $O(CH_2)_3Me$). ^{13}C-NMR (150 MHz, $CDCl_3$): 159.8, 159.7, 159.5, 159.3, 159.2, 159.0, 158.7 (7s, 7 C_{Ar}–OMe); 144.9, 144.7, 136.0 (3*s*, 3 C(1) of MMTr); 130.6–127.0 (several *d* and *s*) and 114.2–113.2 (several *d*) (6 C(1) of PMB, CH's of PMB and MMTr); 106.0 (*d*, C(1'')); 98.8 (*d*, C(1''')); 95.7 (*d*, C(1')); 86.1 (*s*, CAr_3); 84.2 (*d*, C(6)); 82.9 (*d*, C(5)); 82.3 (*d*, C(4'')); 82.1 (*d*, C(2'')); 80.0 (*d*, C(3')); 79.1 (*d*, C(4')); 75.8 (*d*, C(3'')); 75.3, 74.9 (2*t*, 2 ArCH_2); 74.5 (*d*, C(5''')); 74.4 (*d*, C(4)); 73.5, 73.2 (2*t*, 2 ArCH_2); 73.0 (*t*, O$CH_2(CH_2)_2$Me); 72.7 (*d*, C(3''')); 72.2 (*t*, ArCH_2); 71.6 (*d*, C(5')); 71.4 (*t*, ArCH_2); 71.2 (*d*, C(4''')); 70.3 (*t*, C(5'')); 63.6 (*d*, C(2')); 63.1 (*t*, C(6')); 60.6 (*d*, C(1)); 60.3 (*d*, C(3)); 57.4 (*d*, C(2''')); 55.6 (*q*, 2 OMe); 55.5 (*q*, 3 OMe); 55.3, 54.9 (2*q*, 2 OMe); 51.2 (*t*, C(6''')); 32.9 (*t*, C(2)); 32.5 (*t*, $OCH_2CH_2CH_2$Me); 19.4 (*t*, $O(CH_2)_2CH_2$Me); 14.1 (*q*, $O(CH_2)_3Me$). HR-MALDI-MS: 1817.7689 (100, $[M + Na]^+$, $C_{95}H_{107}N_{15}NaO_{21}^+$; calc. 1817.7697).

1,3,2',2''',6'''-Pentazido-1,3,2',2''',6'''-pentadeamino-6,3',2'',5'',3''',4'''-hexakis-O-*(4-methoxybenzyl)-4'*-O-*pentyl-6'*-O-*(monomethoxytrityl)paromomycin* (**7**). Alkylation of 745 mg of **2** with 79.6 µL of 1-bromopentane according to GP1 and FC (hexane/EtOAc 8:2) gave **7** (580 mg, 75%) as colorless viscous oil. R_f (hexane/EtOAc 7:3) 0.55. $[\alpha]_D^{23}$ = +55.5 (*c* = 0.4, $CHCl_3$). IR (ATR): 2933*w*, 2837*w*, 2100*s*, 1611*m*, 1586*w*, 1512*s*, 1463*w*, 1361*w*, 1302*w*, 1246*s*, 1174*m*, 1111*m*, 1070*m*, 1032*s*. ^{1}H-NMR (600 MHz, $CDCl_3$): 7.58–6.58 (*m*, 38 arom. H); 6.27 (*d*, *J* = 3.7, H–C(1')); 5.70 (*d*, *J* = 6.3, H–C(1'')); 4.93 (*d*, *J* = 10.2, ArC*H*); 4.89 (*d*, *J* = 1.8, H–C(1'''));

4.75 and 4.73 (2*d*, *J* = 10.5, ArC*H*$_2$); 4.61 (*d*, *J* = 10.2, ArC*H*); 4.57 (*d*, *J* = 11.0, ArC*H*); 4.56 (*d*, *J* = 11.7, ArC*H*); 4.52 (*d*, *J* = 11.0, ArC*H*); 4.45 (*d*, *J* = 11.3, ArC*H*); 4.42 (*d*, *J* = 11.7, ArC*H*); 4.34 (*d*, *J* = 11.3, ArC*H*); 4.31 (*d*, *J* = 11.7, ArC*H*); 4.29–4.27 (*m*, H–C(4'')); 4.21 (*dd*, *J* = 4.8, 2.0, H–C(3'')); 4.20 (*d*, *J* = 11.3, ArC*H*); 4.12 (*ddd*, *J* = 10.1, 5.2, 1.6, H–C(5')); 4.00–3.97 (*m*, H–C(5), H–C(3'), H–C(2'')); 3.86 (*t*, *J* = 9.6, H–C(4)); 3.83–3.81 (*m*, H$_a$–C(5''), 2 OMe); 3.80, 3.78, 3.75 (3*s*, 3 OMe); 3.74–3.72 (*m*, H–C(3'''), H–C(5''')); 3.66 (*s*, OMe); 3.65–3.61 (*m*, OC*H*$_a$(CH$_2$)$_3$Me); 3.60 (*dd*, *J* = 13.0, 8.7, H$_a$–C(6''')); 3.56 (*dd*, *J* = 10.4, 3.1, H$_b$–C(5'')); 3.50 (*ddd*, *J* = 12.7, 9.6, 4.4, H–C(3)); 3.46–3.41 (*m*, H–C(1), H$_a$–C(6')); 3.40 (br. *s*, H–C(2''')); 3.35 (*s*, OMe); 3.32 (*t*, *J* = 9.4, H–C(6)); 3.31 (*dd*, *J* = 10.1, 9.3, H–C(4')); 3.23–3.19 (*m*, OC*H*$_b$(CH$_2$)$_3$Me); 3.15 (*dd*, *J* = 10.2, 3.7, H–C(2')); 3.13 (*dd*, *J* = 10.2, 5.2, H$_b$–C(6')); 3.07 (br. *s*, H–C(4''')); 2.82 (*dd*, *J* = 13.0, 4.0, H$_b$–C(6''')); 2.23 (*dt*, *J* = 13.1, 4.4, H$_{eq}$–C(2)); 1.39 (*q*, *J* = 12.7, H$_{ax}$–C(2)); 1.31–1.26 (*m*, OCH$_2$C*H*$_2$(CH$_2$)$_2$Me); 1.22–1.16 (*m*, O(CH$_2$)$_3$C*H*$_2$Me); 1.11–0.96 (*m*, O(CH$_2$)$_2$C*H*$_2$CH$_2$Me); 0.81 (*t*, *J* = 7.4, O(CH$_2$)$_4$*Me*). ^{13}C-NMR (150 MHz, CDCl$_3$): 159.8, 159.7, 159.5, 159.3, 159.2, 159.0, 158.7 (7s, 7 *C*$_{Ar}$–OMe); 144.9, 144.6, 136.0 (3*s*, 3 C(1) of MMTr); 130.6–126.9 (several *d* and *s*) and 114.2–113.2 (several *d*) (6 C(1) of PMB, CH's of PMB and MMTr); 106.0 (*d*, C(1'')); 98.8 (*d*, C(1''')); 95.7 (*d*, C(1')); 86.1 (*s*, *C*Ar$_3$); 84.2 (*d*, C(6)); 83.0 (*d*, C(5)); 82.3 (*d*, C(4'')); 82.1 (*d*, C(2'')); 80.0 (*d*, C(3')); 79.0 (*d*, C(4')); 75.8 (*d*, C(3'')); 75.3, 75.0 (2*t*, 2 Ar*C*H$_2$); 74.5 (*d*, C(5''')); 74.4 (*d*, C(4)); 73.52, 73.2 (2*t*, 2 Ar*C*H$_2$); 73.1 (*t*, O*C*H$_2$(CH$_2$)$_3$Me); 72.7 (*d*, C(3''')); 72.1 (*t*, Ar*C*H$_2$); 71.5 (*d*, C(5')); 71.4 (*t*, Ar*C*H$_2$); 71.2 (*d*, C(4''')); 70.2 (*t*, C(5'')); 63.6 (*d*, C(2')); 63.1 (*t*, C(6')); 60.6 (*d*, C(1)); 60.3 (*d*, C(3)); 57.5 (*d*, C(2''')); 55.4 (*q*, 2 OMe); 55.3 (*q*, 3 OMe); 55.2, 54.9 (2*q*, 2 OMe); 51.2 (*t*, C(6''')); 32.9 (*t*, C(2)); 30.0 (*t*, OCH$_2$*C*H$_2$(CH$_2$)$_2$Me); 28.3 (*t*, O(CH$_2$)$_2$*C*H$_2$CH$_2$Me); 22.7 (*t*, O(CH$_2$)$_3$*C*H$_2$Me); 14.1 (*q*, O(CH$_2$)$_4$*Me*). HR-MALDI-MS: 1831.7845 (100, [*M* + Na]$^+$, C$_{96}$H$_{109}$N$_{15}$NaO$_{21}^+$; calc. 1831.7854).

4'-O-*Allyl-1,3,2',2''',6'''-pentazido-1,3,2',2''',6'''-pentadeamino-6,3',2'',5'',3''',4'''-hexakis*-O-*(4-methoxybenzyl)-6'*-O-*(monomethoxytrityl)paromomycin* (**8**). Alkylation of 2.00 g

of **2** with 0.15 mL of allyl bromide according to GP1 and FC (hexane/EtOAc 7:3) gave **8** (1.57 g, 77%) as colorless viscous oil. R_f (hexane/EtOAc 7:3) 0.23. $[\alpha]_D^{23}$ = +51.3 (*c* = 0.65, $CHCl_3$). IR (ATR): 2933*w*, 2836*w*, 2100*s*, 1611*m*, 1585*w*, 1512*s*, 1463*w*, 1359*w*, 1301*w*, 1245*s*, 1173*m*, 1111*m*, 1070*m*, 1033*s*, 909*m*, 818*s*, 728*m*. ^{1}H-NMR (600 MHz, $CDCl_3$): 7.59–6.60 (*m*, 38 arom. H); 6.31 (*d*, *J* = 3.7, H–C(1')); 5.71 (*d*, *J* = 6.3, H–C(1'')); 5.61 (*ddt*, *J* = 17.3, 10.4, 5.7, OCH_2CH=CH_2); 5.04 (*dq*, *J* = 17.2, 1.6, OCH_2CH=CH_Z); 5.00 (*dq*, *J* = 10.4, 1.6, OCH_2CH=CH_E); 4.94 (*d*, *J* = 10.2, ArC*H*); 4.91 (*d*, *J* = 1.8, H–C(1''')); 4.76 (br. *s*, ArCH_2); 4.59 (*d*, *J* = 10.2, ArC*H*); 4.57 (*d*, *J* = 11.4, ArC*H*); 4.55 (*d*, *J* = 11.7, ArC*H*); 4.52 (*d*, *J* = 11.4, ArC*H*); 4.46 (*d*, *J* = 11.5, ArC*H*); 4.43 (*d*, *J* = 11.7, ArC*H*); 4.36 (*d*, *J* = 11.4, ArC*H*); 4.32 (*d*, *J* = 11.7, ArC*H*); 4.30 (*q*, *J* ≈ 2.4, H–C(4'')); 4.22 (*dd*, *J* = 5.0, 2.1, H–C(3'')); 4.21 (*d*, *J* = 11.7, ArC*H*); 4.15 (*ddd*, *J* = 10.3, 5.1, 1.6, H–C(5')); 4.14–4.11 (*m*, CH_aCH=CH_2); 4.03 (*dd*, *J* = 10.4, 9.1, H–C(3')); 4.01–3.98 (*m*, H–C(5), H–C(2'')); 3.85 (*t*, *J* = 9.6, H–C(4)); 3.83–3.81 (*m*, H_a–C(5''), CH_aCH=CH_2, 2 OMe); 3.80, 3.78, 3.76 (3*s*, 3 OMe); 3.75–3.72 (*m*, H–C(3'''), H–C(5''')); 3.67 (*s*, OMe); 3.62 (*dd*, *J* = 13.1, 8.6, H_a–C(6''')); 3.57 (*dd*, *J* = 10.4, 3.0, H_b–C(5'')); 3.50 (*ddd*, *J* = 12.7, 9.8, 4.5, H–C(3)); 3.47–3.43 (*m*, H–C(1), H_a–C(6')); 3.42–3.39 (*m*, H–C(4')); H–C(2''')); 3.34 (*s*, OMe); 3.32 (*t*, *J* = 9.5, H–C(6)); 3.18 (*dd*, *J* = 10.4, 3.7, H–C(2')); 3.14 (*dd*, *J* = 10.0, 5.1, H_b–C(6')); 3.08 (br. *s*, H–C(4''')); 2.83 (*dd*, *J* = 13.1, 4.0, H_b–C(6''')); 2.23 (*dt*, *J* = 13.1, 4.5, H_{eq}–C(2)); 1.39 (*q*, *J* = 12.7, H_{ax}–C(2)). ^{13}C-NMR (150 MHz, $CDCl_3$): 159.8, 159.6, 159.5, 159.3, 159.2, 159.0, 158.7 (7s, 7 C_{Ar}–OMe); 144.9, 144.6, 135.9 (3*s*, 3 C(1) of MMTr); 134.8 (*d*, OCH_2CH=CH_2); 130.6–127.0 (several *d* and *s*) and 114.1–113.2 (several *d*) (6 C(1) of PMB, CH's of PMB and MMTr); 116.7 (*t*, OCH_2CH=CH_2); 106.0 (*d*, C(1'')); 98.8 (*d*, C(1''')); 95.7 (*d*, C(1')); 86.1 (*s*, CAr_3); 84.1 (*d*, C(6)); 83.0 (*d*, C(5)); 82.3 (*d*, C(4'')); 82.1 (*d*, C(2'')); 80.0 (*d*, C(3')); 78.6 (*d*, C(4')); 75.8 (*d*, C(3'')); 75.4, 74.9 (2*t*, 2 ArCH_2); 74.5 (*d*, C(5''')); 74.4 (*d*, C(4)); 73.6 (*t*, OCH_2CH=CH_2); 73.5, 73.2 (2*t*, 2 ArCH_2); 72.6 (*d*, C(3''')); 72.1, 71.4 (2 *t*, 2 ArCH_2); 71.3 (*d*, C(5')); 71.2 (*d*, C(4''')); 70.2 (*t*, C(5'')); 63.6 (*d*, C(2')); 63.1 (*t*, C(6')); 60.6 (*d*, C(1)); 60.3 (*d*, C(3)); 57.5 (*d*, C(2''')); 55.3 (*q*, 2 OMe); 55.25, 55.2, 55.15,

54.7, 53.5 (5*q*, 5 OMe); 51.2 (*t*, C(6’’’)); 32.9 (*t*, C(2)). HR-MALDI-MS: 1801.7376 (100, [*M* + Na]$^+$, $C_{94}H_{103}N_{15}NaO_{21}^+$; calc. 1801.7384).

4’-O-*Methylparomomycin* (**9**) *and its Diacetate* (**9**·2 AcOH). GP 2 (200 mg of **3**) and FC (MeOH/25% aq. NH_3 4:1) gave **9** (41 mg, 60%) as a white powder. R_f (MeOH/ 25% aq. NH_3 4:1) 0.15. IR (ATR): 3103*m*, 2909*m*, 1545*w*, 1403*m*, 1310*w*, 1089*s*, 970*m*. Dissolution of **8** in AcOH/H_2O 1:1, partial evaporation, and lyophilization gave **9**·2 AcOH as a white powder. $[\alpha]_D^{23}$ = +41.3 (*c* = 0.5, H_2O). ^{1}H-NMR (500 MHz, D_2O): 5.81 (*d*, *J* = 4.0, H–C(1’)); 5.42 (*d*, *J* = 2.4, H–C(1’’)); 5.34 (*d*, *J* = 1.6, H–C(1’’’)); 4.58 (*dd*, *J* = 6.8, 4.9, H–C(3’’)); 4.45 (*dd*, *J* = 4.9, 2.4, H–C(2’’)); 4.37 (*ddd*, *J* = 7.0, 3.9, 1.5, H–C(5’’’)); 4.28 (*t*, *J* = 3.2, H–C(3’’’)); 4.25 (*ddd*, *J* = 6.8, 4.7, 3.2, H–C(4’’)); 4.08 (*dd*, *J* = 10.0, 9.2, H–C(4)); 4.05 (*dd*, *J* = 10.7, 9.0, H–C(3’)); 3.96–3.91 (*m*, H_a–C(6’), H_a–C(5’’)); 3.95 (*t*, *J* = 9.2, H–C(5)); 3.86 (*ddd*, *J* = 3.2, 2.0, 1.3, H–C(4’’’)); 3.83–3.78 (*m*, H–C(5’), H_b–C(6’), H_b–C(5’’)); 3.78 (*dd*, *J* = 10.5, 9.3, H–C(6)); 3.63 (*ddd*, *J* = 3.0, 1.7, 1.2, H–C(2’’’)); 3.60 (*s*, OMe); 3.60–3.55 (*m*, H–C(3)); 3.47 (*dd*, *J* = 10.7, 4.0, H–C(2’)); 3.46 (*dd*, *J* = 13.6, 7.1, H_a–C(6’’’)); 3.41–3.36 (*m*, H–C(1)); 3.39 (*dd*, *J* = 13.6, 3.9, H_b–C(6’’’)); 3.31 (*t*, *J* = 9.1, H–C(4’)); 2.51 (*dt*, *J* = 12.6, 4.3, H_{eq}–C(2)); 1.94 (*s*, 2 $MeCO_2^-$); 1.92 (*q*, *J* = 12.6, H_{ax}–C(2)). ^{13}C-NMR (125 MHz, D_2O): 181.8 (*s*, Me*C*O_2^-); 109.8 (*d*, C(1’’)); 95.6 (*d*, C(1’)); 95.3 (*d*, C(1’’’)); 84.0 (*d*, C(5)); 81.1 (*d*, C(4’’)); 78.7 (*d*, C(4’)); 77.7 (*d*, C(4)); 74.7 (*d*, C(3’’)); 73.0 (*d*, C(2’’)); 72.9 (*d*, C(5’)); 72.1 (*d*, C(6)); 70.2 (*d*, C(5’’’)); 68.7 (*d*, C(3’)); 67.5 (*d*, C(3’’’)); 67.0 (*d*, C(4’’’)); 60.4 (*q*, OMe); 60.0 and 59.8 (2*t*, C(6’), C(5’’)); 53.6 (*d*, C(2’)); 50.7 (*d*, C(2’’’)); 49.7 (*d*, C(1)); 48.7 (*d*, C(3)); 40.2 (*t*, C(6’’’)); 29.7 (*t*, C(2)); 22.8 (*q*, *Me*CO_2^-). HR-MALDI-MS: 630.3195 (100, [*M* + Na]$^+$, $C_{24}H_{47}N_5$ Na O_{14}^+; calc. 630.3192).

4’-O-*Ethylparomomycin* (**10**) *and its Pentacetate* **10**·5 AcOH. GP 2 (200 mg of **4**) and FC (MeOH/ 25% aq. NH_3 4:1) gave **10** (47 mg, 64%) as a white powder. R_f (MeOH/25% aq. NH_3 4:1) 0.16. IR (ATR): 3103*m*, 2909*m*, 1545*w*, 1403*m*, 1310*w*, 1089*s*, 970*m*. Dissolution of **10** in AcOH/H_2O 1:1, partial evaporation, and lyophilization gave **10**·5 AcOH as a white powder. $[\alpha]_D^{23}$ = +29.3 (*c* = 0.3, H_2O). ^{1}H-NMR (600 MHz, D_2O): 5.73 (*d*, *J* = 3.9, H–C(1’)); 5.41 (*d*, *J* =

2.3, H–C(1'')); 5.32 (*d*, *J* = 1.6, H–C(1''')); 4.57 (*dd*, *J* = 6.6, 4.9, H–C(3'')); 4.43 (*dd*, *J* = 4.9, 2.4, H–C(2'')); 4.36 (*ddd*, *J* = 7.0, 4.0, 1.7, H–C(5''')); 4.26 (*t*, *J* = 3.1, H–C(3''')); 4.24 (*ddd*, *J* = 6.8, 4.9, 2.4, H–C(4'')); 3.96 (*dd*, *J* = 10.6, 9.2, H–C(3')); 3.96–3.75 (*m*, H–C(4), H–C(5), H–C(5'), $H_2C(6')$, $H_2C(5'')$, H–C(4'''), O*C*H_2Me); 3.69 (*dd*, *J* = 10.2, 9.4, H–C(6)); 3.60 (br. *s*, H–C(2''')); 3.46 (*dd*, *J* = 13.6, 7.0, H_a–C(6''')); 3.42–3.37 (*m*, H–C(4'), H_b–C(6''')); 3.38 (*dd*. *J* = 10.5, 3.9, H–C(2')); 3.315–3.27 (*m*, H–C(1)); 3.292–3.25 (*m*, H–C(3)); 2.34 *(dt*, *J* = 12.7, 4.4, H_{eq}–C(2)); 1.94 (*s*, 5 $MeCO_2^-$); 1.70 (*q*, *J* = 12.7, H_{ax}–C(2)); 1.23 (*t*, *J* = 7.1, OCH_2*Me*). ^{13}C-NMR (150 MHz, D_2O): 181.4 (*s*, Me*C*O_2^-); 109.9 (*d*, C(1'')); 96.1 (*d*, C(1')); 95.5 (*d*, C(1''')); 84.6 (*d*, C(5)); 81.1 (*d*, C(4'')); 80.0 (*d*, C(4)); 77.4 (*d*, C(4')); 75.0 (*d*, C(3'')); 73.2 (*d*, C(2'')); 73.0 (*d*, C(6)); 72.7 (*d*, C(5')); 70.3 (*d*, C(5''')); 69.5 (*d*, C(3')); 69.3 (*t*, O*C*H_2Me); 67.8 (*d*, C(3''')); 67.3 (*d*, C(4''')); 60.1 (*t*, C(5'')); 59.9 (*t*, C(6')); 54.1 (*d*, C(2')); 50.9 (*d*, C(2''')); 50.2 (*d*, C(1)); 49.1 (*d*, C(3)); 40.4 (*t*, C(6''')); 30.3 (*t*, C(2)); 23.2 (*q*, *Me*CO_2^-); 14.6 (*q*, OCH_2*Me*). HR-MALDI-MS: 666.3158 (100, $[M + Na]^+$, $C_{25}H_{49}N_5NaO_{14}^+$; calc. 666.3168).

4'-O-*Propylparomomycin* (**11**) *and its Sesquiacetate* **11**·1.5 AcOH. GP 2 (200 mg of **5**) and FC (MeOH/25% aq. NH_3 4:1) gave **11** (36 mg, 49%) as a white powder. R_f (MeOH/ 25% aq. NH_3 4:1) 0.20. IR (ATR): 3165*m*, 2919*m*, 1662*m*, 1613*m*, 1531*w*, 1402*m*, 1046*s*, 970*m*. Dissolution of **11** in AcOH/H_2O 1:1, partial evaporation, and lyophilization gave **11**·1.5 AcOH as a white powder. $[\alpha]_D^{23}$ = +37.8 *(c* = 0.24, H_2O). ^{1}H-NMR (500 MHz, D_2O): 5.80 (*d*, *J* = 3.9, H–C(1')); 5.41 (*d*, *J* = 2.3, H–C(1'')); 5.33 (*d*, *J* = 1.6, H–C(1''')); 4.57 (*dd*, *J* = 6.8, 4.9, H–C(3'')); 4.45 (*dd*, *J* = 4.8, 2.3, H–C(2'')); 4.36 (*ddd*, *J* = 7.0, 3.9, 1.4, H–C(5''')); 4.27 (*t*, *J* = 3.1, H–C(3''')); 4.24 (*ddd*, *J* = 6.8, 4.6, 2.9, H–C(4'')); 4.05 (*t*, *J* = 9.4, H–C(4)); 4.01 (*dd*, *J* = 10.7, 9.2, H–C(3')); 3.95 (*t*, *J* = 9.1, H–C(5)); 3.95–3.90 (*m*, H_a–C(6'), H_a–C(5'')); 3.85–3.83 (*m*, H–C(4''')); 3.82–3.74 (*m*, H–C(6), H–C(5'), H_b–C(6'), H_b–C(5''), O*C*$H_a$$CH_2$Me); 3.67–3.63 (*m*, H–C(2'''), O*C*$H_b$$CH_2$Me); 3.59–3.53 (*m*, H–C(3)); 3.46–3.41 (*m*, H_a–C(6''')); 3.45 (*dd*, *J* = 10.5, 3.8, H–C(2')); 3.40–3.34 (*m*, H–C(3), H–C(4'), H_b–C(6''')); 2.50 (*dt*, *J* = 12.7, 4.2, H_{eq}–C(2)); 1.93 (*s*, 1.5 $MeCO_2^-$); 1.90 (*q*, *J* = 12.7, H_{ax}–C(2)); 1.60 (*sextet*, *J* = 7.3, OCH_2CH_2Me);

0.91 (*t*, *J* = 7.4, O(CH$_2$)$_2$*Me*). ^{13}C-NMR (125 MHz, D$_2$O): 180.8 (*s*, Me*C*O$_2^-$); 109.8 (*d*, C(1'')); 95.6 (*d*, C(1')); 94.9 (*d*, C(1''')); 83.9 (*d*, C(5)); 81.0 (*d*, C(4'')); 77.7 (*d*, C(4)); 77.2 (*d*, C(4')); 75.4 (*t*, O*C*H$_2$CH$_2$Me); 74.6 (*d*, C(3'')); 72.9 (*d*, C(2'')); 72.8 (*d*, C(6)); 72.0 (*d*, C(5')); 70.1 (*d*, C(5''')); 68.8 (*d*, C(3')); 67.4 (*d*, C(3''')); 66.9 (*d*, C(4''')); 59.84 and 59.77 (2*t*, C(6'), C(5'')); 53.7 (*d*, C(2')); 50.6 (*d*, C(2''')); 49.6 (*d*, C(1)); 48.7 (*d*, C(3)); 40.1 (*t*, C(6''')); 28.1 (*t*, C(2)); 22.8 (*q*, *Me*CO$_2^-$); 22.4 (*t*, OCH$_2$*C*H$_2$Me); 9.5 (*q*, O(CH$_2$)$_2$*Me*). HR-MALDI-MS: 680.3323 (25, [*M* + Na]$^+$, $C_{26}H_{51}N_5NaO_{14}^+$; calc. 680.3325), 658.3504 (100, [*M* + H]$^+$, $C_{26}H_{52}N_5O_{14}^+$; calc. 658.3505).

4'-O-*Butylparomomycin* (**12**) *and its Acetate* **12**·0.4 AcOH. GP 2 (200 mg of **6**) and FC (MeOH/25% aq. NH$_3$ 4:1) gave **12** (48 mg, 64%) as a white powder. R_f (MeOH/ 25% aq. NH$_3$ 4:1) 0.22. IR (ATR): 3146*m*, 2922*m*, 1665*m*, 1611*m*, 1530*w*, 1423*m*, 1103*s*. Dissolution of **12** in AcOH/H$_2$O 1:1, partial evaporation, and lyophilization gave **12**·0.4 AcOH as a white powder. $[\alpha]_D^{23}$ = +33.2 (*c* = 0.6, H$_2$O). ^{1}H-NMR (600 MHz, D$_2$O): 5.80 (*d*, *J* = 4.0, H–C(1')); 5.42 (*d*, *J* = 2.3, H–C(1'')); 5.34 (*d*, *J* = 1.8, H–C(1''')); 4.58 (*dd*, *J* = 6.7, 4.9, H–C(3'')); 4.46 (*dd*, *J* = 4.9, 2.3, H–C(2'')); 4.37 (*ddd*, *J* = 7.0, 3.8, 1.3, H–C(5''')); 4.28 (*t*, *J* = 3.1, H–C(3''')); 4.25 (*ddd*, *J* = 6.8, 4.5, 3.1, H–C(4'')); 4.04–3.99 (*m*, H–C(4), H–C(3')); 3.97–3.91 (*m*, H–C(5), H$_a$–C(6'), H$_a$–C(5'')); 3.89–3.85 (*m*, H–C(4'''), OC*H*$_a$(CH$_2$)$_2$Me); 3.84–3.78 (*m*, H–C(5'), H$_b$–C(6'), H$_b$–C(5'')); 3.77 (*dd*, *J* = 10.0, 9.3, H–C(6)); 3.71 (*dt*, *J* = 9.4, 6.8, OC*H*$_b$(CH$_2$)$_2$Me); 3.63 (br. *d*, *J* = 0.9, H–C(2''')); 3.54–3.49 (*m*, H–C(3)); 3.48–3.44 (*m*, H–C(2'), H$_a$–C(6''')); 3.42–3.35 (*m*, H–C(1), H–C(4'), H$_b$–C(6''')); 2.48 (*dt*, *J* = 12.6, 4.4, H$_{eq}$–C(2)); 1.94 (*s*, 0.4 MeCO$_2^-$); 1.88 (*q*, *J* = 12.6, H$_{ax}$–C(2)); 1.63–1.55 (*m*, OCH$_2$C*H*$_2$CH$_2$Me); 1.40–1.34 (*m*, O(CH$_2$)$_2$C*H*$_2$Me); 0.92 (*t*, *J* = 7.4, O(CH$_2$)$_3$*Me*). ^{13}C-NMR (150 MHz, D$_2$O): 181.1 (*s*, *Me*CO$_2^-$); 110.0 (*d*, C(1'')); 95.9 (*d*, C(1')); 95.2 (*d*, C(1''')); 84.2 (*d*, C(5)); 81.2 (*d*, C(4'')); 78.2 (*d*, C(4)); 77.5 (*d*, C(4')); 74.9 (*d*, C(3'')); 73.7 (*t*, O*C*H$_2$(CH$_2$)$_2$Me); 73.2 (*d*, C(2'')); 73.1 (*d*, C(5')); 72.3 (*d*, C(6)); 70.3 (*d*, C(5''')); 69.1 (*d*, C(3')); 67.7 (*d*, C(3''')); 67.1 (*d*, C(4''')); 60.1 and 60.0 (2*t*, C(6'), C(5'')); 54.0 (*d*, C(2')); 50.8 (*d*, C(2''')); 49.9 (*d*, C(1)); 48.9 (*d*, C(3)); 40.4 (*t*, C(6''')); 31.3 (*t*,

$OCH_2CH_2CH_2Me$); 28.7 (*t*, C(2)); 23.0 (*q*, $MeCO_2^-$); 18.5 (*t*, $O(CH_2)_2CH_2Me$); 13.0 (*q*, $O(CH_2)_3Me$). HR-MALDI-MS: 672.3653 (100, $[M + H]^+$, $C_{27}H_{54}N_5O_{14}^+$; calc. 672.3662).

4'-O-Pentylparomomycin (**13**). GP 2 (200 mg of **7**) and FC (MeOH/25% aq. NH_3 4:1) gave **13** (57 mg, 75%) as a white powder. R_f (MeOH/ 25% aq. NH_3 4:1) 0.30. IR (ATR): 3169*m*, 2938*m*, 1622*m*, 1523*w*, 1419*m*, 1110*s*. Dissolution of **13** in AcOH/H_2O 1:1, partial evaporation, and lyophilization gave **13** as a white powder. $[\alpha]_D^{23}$ = +30.4 (*c* = 0.31, H_2O). ^{1}H-NMR (500 MHz, D_2O): 5.77 (*d*, *J* = 4.0, H–C(1')); 5.37 (*d*, *J* = 2.0, H–C(1'')); 5.28 (br. *s*, H–C(1''')); 4.52 (*dd*, *J* = 6.4, 5.1, H–C(3'')); 4.40 (*dd*, *J* = 4.7, 2.2, H–C(2'')); 4.33–4.30 (*m*, H–C(5''')); 4.23 (*t*, *J* = 3.1, H–C(3''')); 4.21–4.17 (*m*, H–C(4'')); 4.05 (*t*, *J* = 9.6, H–C(4)); 3.97 (*dd*, *J* = 10.0, 9.6, H–C(3')); 3.94–3.86 (*m*, H–C(5), H_a–C(6'), H_a–C(5'')); 3.82–3.78 (*m*, H–C(4'''), $CH_a(CH_2)_3Me$); 3.77–3.72 (*m*, H–C(6), H–C(5'), H_b–C(6'), H_b–C(5'')); 3.64 (*dt*, *J* = 9.1, 6.9, $CH_b(CH_2)_3Me$); 3.60–3.54 (*m*, H–C(3), H–C(2''')); 3.42 (*dd*, *J* = 10.0, 4.0, H–C(2')); 3.40 (*dd*, *J* = 13.5, 6.9, H_a–C(6''')); 3.37–3.33 (*m*, H–C(1), H–C(4')); 3.34 (*dd*, *J* = 13.5, 3.9, H_b–C(6''')); 2.49 (*dt*, *J* = 12.6, 4.0, H_{eq}–C(2)); 1.91 (*q*, *J* = 12.5, H_{ax}–C(2)); 1.58–1.52 (*m*, $OCH_2CH_2(CH_2)_2Me$); 1.29–1.25 (*m*, $O(CH_2)_2(CH_2)_2Me$); 0.83 (*t*, *J* = 6.9, $O(CH_2)_4Me$). ^{13}C-NMR (150 MHz, D_2O): 110.0 (*d*, C(1'')); 95.9 (*d*, C(1')); 95.3 (*d*, C(1''')); 84.1 (*d*, C(5)); 81.3 (*d*, C(4'')); 77.7 (*d*, C(4)); 77.5 (*d*, C(4')); 75.0 (*d*, C(3'')); 74.0 (*t*, $OCH_2(CH_2)_3Me$); 73.3 (*d*, C(2'')); 73.2 (*d*, C(5')); 72.2 (*d*, C(6)); 70.4 (*d*, C(5''')); 69.0 (*d*, C(3')); 67.7 (*d*, C(3''')); 67.2 (*d*, C(4''')); 60.2 and 60.1 (2*t*, C(6'), C(5'')); 53.9 (*d*, C(2')); 50.9 (*d*, C(2''')); 49.8 (*d*, C(1)); 49.0 (*d*, C(3)); 40.4 (*t*, C(6''')); 28.9 (*t*, $OCH_2CH_2(CH_2)_2Me$); 28.0 (*t*, C(2)); 27.5 (*t*, $O(CH_2)_2CH_2CH_2Me$); 21.8 (*t*, $O(CH_2)_3CH_2Me$); 13.3 (*q*, $O(CH_2)_4Me$). HR-MALDI-MS: 686.3827 (100, $[M + H]^+$, $C_{28}H_{56}N_5O_{14}^+$; calc. 686.3818).

4'-O-*Allylparomomycin* (**14**) *and its Acetate* **14**·3.5 AcOH. GP 2 (200 mg of **13**) and FC (MeOH/25% aq. NH_3 4:1) gave **14** (41 mg, 55%) as a white powder. R_f (MeOH/25% aq. NH_3 4:1) 0.29. IR (ATR): 3284*m*, 2916*m*, 1567*m*, 1417*m*, 1392*m*, 1427*m*, 1110*s*. Dissolution of **14** in AcOH/H_2O 1:1, partial evaporation, and lyophilization gave **14**·3.5 AcOH as a white powder.

$[\alpha]_D^{23}$ = +29.3 (*c* = 0.22, H_2O). ^{1}H-NMR (600 MHz, D_2O): 6.01 (*ddt*, *J* = 17.2, 10.4, 6.2, OCH_2CH=CH_2); 5.76 (*d*, *J* = 3.9, H–C(1')); 5.41 (*d*, *J* = 2.4, H–C(1'')); 5.38 (*dq*, *J* = 17.2, 1.4, OCH_2CH=CH_Z); 5.33 (*d*, *J* = 1.7, H–C(1''')); 5.31 (*dq*, *J* = 10.4, 1.4, OCH_2CH=CH_E); 4.56 (*dd*, *J* = 6.7, 5.0, H–C(3'')); 4.41 (*dd*, *J* = 5.0, 2.4, H–C(2'')); 4.37–4.33 (*m*, H–C(5'''), OCH_aCH=CH_2); 4.27 (*t*, *J* = 3.1, H–C(3''')); 4.25–4.23 (*m*, H–C(4''), OCH_bCH=CH_2); 4.02 (*dd*, *J* = 10.5, 9.0, H–C(3')); 3.95 (*dd*, *J* = 12.3, 3.0, H_a–C(6')); 3.93 (*dd*, *J* = 12.6, 2.8, H_a–C(5'')); 3.88 (*t*, *J* = 9.0, H–C(5)); 3.87–3.85 (*m*, H–C(4), H–C(5')); 3.85–3.82 (*m*, H–C(4''')); 3.82 (*dd*, *J* = 12.6, 4.8, H_b–C(5'')); 3.81 (*dd*, *J* = 12.3, 4.8, H_b–C(6')); 3.66 (*dd*, *J* = 10.4, 9.0, H–C(6)); 3.62 (*dd*, *J* = 3.1, 1.7, H–C(2''')); 3.48 (*dd*, *J* = 9.4, 9.0, H–C(4')); 3.47 (*dd*, *J* = 13.6, 6.8, H_a–C(6''')); 3.42 (*dd*, *J* = 10.5, 3.9, H–C(2')); 3.40 (*dd*, *J* = 13.6, 3.9, H_b–C(6''')); 3.35–3.29 (*m*, H–C(1), H–C(3)); 2.38 (*dt*, *J* = 12.7, 4.2, H_{eq}–C(2)); 1.94 (*s*, 3.5 $MeCO_2^-$); 1.71 (*q*, *J* = 12.7, H_{ax}–C(2)). ^{13}C-NMR (150 MHz, D_2O): 180.9 (*s*, $MeCO_2^-$); 133.5 (*d*, OCH_2CH=CH_2); 118.7 (*t*, OCH_2CH=CH_2); 109.7 (*d*, C(1'')); 95.7 (*d*, C(1')); 95.3 (*d*, C(1''')); 84.4 (*d*, C(5)); 81.1 (*d*, C(4'')); 79.3 (*d*, C(4)); 76.7 (*d*, C(4')); 75.1 (*d*, C(3'')); 73.9 (*t*, OCH_2CH=CH_2), 73.2 (*d*, C(2'')); 72.71 (*d*, C(5')); 72.65 (*d*, C(6)); 70.1 (*d*, C(5''')); 69.2 (*d*, C(3')); 67.5 (*d*, C(3''')); 67.1 (*d*, C(4''')); 60.0 and 59.8 (2*t*, C(6'), C(5'')); 53.8 (*d*, C(2')); 50.7 (*d*, C(2''')); 49.9 (*d*, C(1)); 48.8 (*d*, C(3)); 40.2 (*t*, C(6''')); 29.9 (*t*, C(2)); 22.9 (*q*, $MeCO_2^-$). HR-MALDI-MS: 656.3352 (100, [*M* + H]$^+$, $C_{26}H_{50}N_5O_{14}^+$; calc. 656.3349).

1,3,2',2''',6'''-Pentazido-1,3,2',2''',6'''-pentadeamino-4'-O-(3-hydroxypropyl)-6,3',2'',5'',3''',4'''-hexakis-O-(4-methoxybenzyl)-6'-O-(monomethoxytrityl)paromo-mycin (**23**). A soln. of **14** (120 mg, 0.07 mmol) in THF (2 mL) under N_2 at 0 °C was treated with $BH_3{\cdot}SMe_2$ (51 µL, 0.1 mmol). The mixture was stirred at 26 °C for 2 h, cooled to 0 °C , treated with 0.1 N NaOH (4.1 mL, 0.42 mmol) and 30% H_2O_2 (42 µL, 0.42 mmol), stirred at 26 °C for 2 h, and extracted with EtOAc (3 x). The combined organic phases were washed with water and brine, dried (Na_2SO_4), filtered, and evaporated. FC (pentane/EtOAc 6:4) gave **23** (78 mg, 64%) as colorless viscous oil. R_f (pentane/EtOAc 6:4) 0.29. $[\alpha]_D^{23}$ = +48.2 (*c* = 0.3, $CHCl_3$). IR (ATR):

3203*w*, 2934*w*, 2837*w*, 2100*s*, 1611*m*, 1586*w*, 1512*s*, 1463*w*, 1363*w*, 1302*w*, 1245*s*, 1174*m*, 1070*m*, 1035*s*, 908*m*, 818*s*, 728*m*. ^{1}H-NMR (600 MHz, $CDCl_3$): 7.58–6.58 (*m*, 38 arom. H); 6.29 (*d*, *J* = 3.8, H–C(1')); 5.70 (*d*, *J* = 6.3, H–C(1'')); 4.93 (*d*, *J* = 10.2, ArC*H*); 4.89 (*d*, *J* = 1.8, H–C(1''')); 4.76 and 4.74 (2*d*, *J* = 10.3, ArCH_2); 4.62 (*d*, *J* = 10.2, ArC*H*); 4.57, 4.56 (2*d*, *J* = 11.7, 2 ArC*H*); 4.51, 4.45 (2*d*, *J* = 11.3, 2 ArC*H*); 4.42 (*d*, *J* = 11.7, ArC*H*); 4.35 (*d*, *J* = 11.3, ArC*H*); 4.30 (*d*, *J* = 11.7, ArC*H*); 4.28 (*q*, *J* ≈ 2.4, H–C(4'')); 4.21 (*dd*, *J* = 4.8, 2.1, H–C(3'')); 4.19 (*d*, *J* = 11.7, ArC*H*); 4.10 (*ddd*, *J* = 10.2, 4.9, 1.5, H–C(5')); 4.00 (*dd*, *J* = 10.3, 8.9, H–C(3')); 3.99–3.96 (*m*, H–C(5), H–C(2'')); 3.82 (*dd*, *J* = 9.6, 9.1, H–C(6)); 3.81–3.80 (*m*, H_a–C(5''), 2 OMe, OCH_aCH_2CH_2OH); 3.79, 3.78, 3.75 (3*s*, 3 OMe); 3.74–3.72 (*m*, H–C(3'''), H–C(5''')); 3.66 (*s*, OMe); 3.61 (*dd*, *J* = 12.9, 8.4, H_a–C(6''')); 3.55 (*dd*, *J* = 10.4, 3.1, H_b–C(5'')); 3.52–3.45 (*m*, H–C(3), H_a–C(6')); 3.43–3.36 (*m*, H–C(1), H–C(4'), H–C(2'''), OCH_bCH_2CH_2OH); 3.33 (*s*, OMe); 3.30 (*t*, *J* = 9.5, H–C(6)); 3.15–3.13 (*m*, H–C(2'), H_b–C(6')); 3.07 (br. *s*, H–C(4''')); 2.82 (*dd*, *J* = 12.9, 4.0, H_b–C(6''')); 2.22 (*dt*, *J* = 13.1, 4.5, H_{eq}–C(2)); 1.69 (br. *s*, OH); 1.58–1.55 (*m*, OCH_2CH_aCH_2OH); 1.47–1.44 (*m*, OCH_2CH_bCH_2OH); 1.36 (*q*, *J* = 12.9, H_{ax}–C(2)). ^{13}C-NMR (150 MHz, $CDCl_3$): 159.8, 159.7, 159.5, 159.4, 159.2, 159.0, 158.8(7s, 7 C_{Ar}–OMe); 144.8, 144.5,135.9 (3*s*, 3 C(1) of MMTr); 130.6–127.0 (several *d* and *s*) and 114.2–113.3 (several *d*) (6 C(1) of PMB, CH's of PMB and MMTr); 106.1 (*d*, C(1'')); 98.8 (*d*, C(1''')); 95.8 (*d*, C(1')); 86.2 (*s*, *C*Ar_3); 84.2 (*d*, C(6)); 83.0 (*d*, C(5)); 82.4 (*d*, C(4'')); 82.0 (*d*, C(2'')); 79.9 (*d*, C(3')); 79.2 (*d*, C(4')); 75.8 (*d*, C(3'')); 75.4, 75.0 (2*t*, 2 Ar*C*H_2); 74.6 (*d*, C(4)); 74.5 (*d*, C(5''')); 73.5, 73.3 (2*t*, 2 Ar*C*H_2); 72.7 (*d*, C(3''')); 72.1 (*t*, O*C*H_2(CH_2)$_2$OH); 71.7 (*t*, Ar*C*H_2); 71.3 (*d* and *t*, C(5'), Ar*C*H_2); 71.2 (*d*, C(4''')); 70.2 (*d*, C(5'')); 63.5 (*d*, C(2')); 62.8 (*t*, C(6')); 61.4 (*t*, O(CH_2)$_2$*C*H_2OH); 60.6 (*d*, C(1)); 60.3 (*d*, C(3)); 57.5 (*d*, C(2''')); 55.4 (*q*, 3 OMe); 55.3 (*q*, 2 OMe); 55.2, 54.9 (2*q*, 2 OMe); 51.3 (*t*, C(6''')); 32.9 (*t*, C(2)); 32.6 (*t*, OCH_2*C*H_2CH_2OH). HR-MALDI-MS: 1819.7451 (100, [*M* + Na]$^+$, $C_{94}H_{105}N_{15}NaO_{22}^+$; calc. 1819.7490).

4'-O-*(3-Hydroxypropyl)paromomycin* (**15**) *and its Decaacetate* **15**·10 AcOH. GP 2 (165 mg of **23**) and FC (MeOH/25% aq. NH_3 4:1) gave **16** (39 mg, 52%) as a white powder. R_f (MeOH/25% aq. NH_3 4:1) 0.19. IR (ATR): 3203*m*, 2909*m*, 1568*m*, 1403*m*, 1395*m*, 1108*s*. Dissolution of **15** in AcOH/H_2O 1:1, partial evaporation, and lyophilization gave **15**·10 AcOH as a white powder. $[\alpha]_D^{23}$ = +28.8 (*c* = 0.25, H_2O). ^{1}H-NMR (600 MHz, D_2O): 5.65 (*d*, *J* = 3.9, H–C(1')); 5.41 (*d*, *J* = 2.4, H–C(1'')); 5.26 (*d*, *J* = 1.7, H–C(1''')); 4.56 (*dd*, *J* = 6.7, 4.9, H–C(3'')); 4.41 (*dd*, *J* = 4.9, 2.3, H–C(2'')); 4.34–4.32 (*m*, H–C(5''')); 4.24–4.21 (*m*, H–C(4''), H–C(3''')); 3.98–3.86 (*m*, H–C(3'), H–C(5'), H_a–C(6'), H_a–C(5''), OC$H_a$$CH_2CH_2OH$); 3.85–3.77 (*m*, H–C(5), H_b–C(6'), H_b–C(5''), H–C(4'''), OC$H_b$$CH_2CH_2OH$); 3.71 (*td*, *J* = 6.4, 1.5, $OCH_2CH_2CH_2OH$); 3.67 (*t*, *J* = 9.4, H–C(4)); 3.60 (*dd*, *J* = 10.5, 9.6, H–C(6)); 3.48 (br. *s*, H–C(2''')); 3.44 (*dd*, *J* = 13.6, 7.2, H_a–C(6''')); 3.40 (*d*, *J* = 9.6, 9.2, H–C(4')); 3.39 (*dd*, *J* = 13.6, 3.9, H_b–C(6''')); 3.24 (*dd*, J = 10.7, 3.9, H–C(2')); 3.23–3.18 (*m*, H–C(1)); 3.12 (*ddd*, *J* = 12.6, 9.5, 4.5, H–C(3)); 2.24 (*dt*, *J* = 12.6, 4.5, H_{eq}–C(2)); 1.94 (*s*, 10 $MeCO_2^-$); 1.90–1.86 (*m*, $OCH_2CH_2CH_2OH$); 1.55 (*q*, *J* = 12.6, H_{ax}–C(2)). ^{13}C-NMR (150 MHz, D_2O): 181.2 (*s*, $MeCO_2^-$); 109.4 (*d*, C(1'')); 96.6 (*d*, C(1')); 96.2 (*d*, C(1''')); 84.4 (*d*, C(5)); 81.0 (*d*, C(4), C(4'')); 77.7 (*d*, C(4')); 75.0 (*d*, C(3'')); 73.5 (*d*, C(6)); 73.1 (*d*, C(2'')); 72.2 (*d*, C(5')); 70.3 (*d*, C(5''')); 70.1 (*d* and *t*, C(3'), O$CH_2CH_2CH_2OH$); 68.2 (*d*, C(3''')); 67.4 (*d*, C(4''')); 60.1 and 59.9 (2*t*, C(6'), C(5'')); 58.4 (*t*, $OCH_2CH_2CH_2OH$); 54.3 (*d*, C(2')); 51.1 (*d*, C(2''')); 50.2 (*d*, C(1)); 49.1 (*d*, C(3)); 40.3 (*t*, C(6''')); 31.6 (*t*, $OCH_2CH_2CH_2OH$); 31.5 (*t*, C(2)); 23.0 (*q*, $MeCO_2^-$). HR-MALDI-MS: 674.3458 (100, $[M + H]^+$, $C_{26}H_{52}N_5O_{15}^+$; calc. 674.3454).

4'-O-(2-Hydroxyethyl)paromomycin (**16**). A soln. of 5.0 g (1 eq.) **24** (1) in 15 mL DMF was added over 15 min to a suspension of 0.43 g 60% NaH in mineral oil (3.0 eq.). The mixture was cooled to 0° C, tetrabutyl ammonium iodide (TBAI, 0.14 g, 0.1 eq) was added, and the mixture was stirred for 1 h at 0°C. A soln. of 3.1 g (3.0 eq.) **25** in 5 mL DMF was added over 5 min. Stirring was continued for 24h, the temperature increasing to r.t., when 20 mL satd. aq. NH_4Cl was added, followed by extraction with t.-butyl-methyl ether (TBME). The org. phase

was processed as usual to leave 6.9 g crude. Chromatography on silica gel (230-400 mesh) (15% EtOAc in hexanes) provided 3.2g (58%) *1,3,2',2''',6'''-Pentazido-1,3,2',2''',6'''-pentadeamino-6,3',2'',5'',3''',4'''-hexakis*-O-*(benzyl)-4'*-O-*[(2,2-dimethyl-1,3-dioxolane-4-methylenyl)]–paromomycin* (**26**) as a pale brown oil. A soln. of a 2.5 g aliquot of his material (1 eq.) in 25 mL 1:1 CH_2Cl_2/MeOH at 0°C was treated with a soln. of 0.32 g (1 eq.) $TsOH \cdot H_2O$ in 1 mL MeOH. The mixture was stirred at 0°C for 15 min., allowed to reach r.t., stirred for 24 h, treated with 15 mL satd. aq. NaHCO3, and extracted with CH_2Cl_2. The org. phase was proceeded as usual to yield 2.5 g crude that was purified by silica gel chromatography (12% EtOAc in hexanes) to provide 1.75 g (72%) of *1,3,2',2''',6'''-Pentazido-1,3,2',2''',6'''-pentadeamino-6,3',2'',5'',3''',4'''-hexakis*-O-*(benzyl)-4'*-O-*[(2,3-dihydroxy)propyl]-paromomycin* (**27)**. A soln. of 1.7 g **27** (1.0 eq) in 22.1 mL THF. 5.1 mL H_2O, and 0.7 mL satd. aq. $NaHCO_3$ at 0° was slowly treated with 1.25 g (5.0 eq) $NaIO_4$. The mixture was stirred for 4h, and diluted with 20 mL EtOAc. The org. phase was separated, and the aq. phase extracted with 2x 20 mL EtOAc. The org. phases were processed as usual to provide 1.5 g crude that was purified by chromatography on silica (12% EtOAc in hexanes) to yield 1.4 g pale oil that was taken up in 14 ml MeOH and 1.4 mL CH_2Cl_2. The soln. was cooled to 0°C, treated with 0.37 g $NaBH_4$ (10 eq.), stirred for 15 min, and diluted with 10 mL EtOAc and 10 mL H_2O. Layers were separated. The aq. phase was extracted with EtOAc. The org. phases were processed as usual to provide 1.3 g crude that was purified by chromatography on silica (60-120 mesh) (20% EtOAc in hexanes) to provide 1.1 g of (79%) *1,3,2',2''',6'''-Pentazido-1,3,2',2''',6'''-pentadeamino-6,3',2'',5'',3''',4'''-hexakis*-O-*(benzyl)-4'*-O-*(2-hydroxy)propy)-paromomycin* (**28**). A HAST reactor was charged with 1.1 g $Pd(OH)_2$ and 4.4 mL 50% aq. MeOH. The mixture was stirred under H_2 (15 mbar) at r.t. for 30 min. A soln. of 1.1g **28** (1.0 eq) in 2.2 mL THF and 0.6 mL AcOH was added, and the mixture was stirred for 96 h under H_2 (25 mbar) and filtered through Celite (bed washed with 25 mL H_2O). The filtrate was taken to dryness, leaving 1.2 g crude that was purified by chromatography on neutralized silica (60–120 mesh) (10% NH_3 in MeOH) to

provide 210 mg crude that was filtered through sephadex. The filtrate was lyophilized to leave 95 mg of a colorless solid that was co-evaporated with 20% aq. AcOH to provide 82 mg of **16** (11%). $[\alpha]_D^{24}$= +39.2 (c = 0.29, H_2O). ^{1}H-NMR (600 MHz, D_2O): 5.60 (*d*, *J* = 4.1, H–C(1')); 5.24 (*d*, *J* = 2.6, H–C(1'')); 5.14 (*d*, *J* = 1.5, H–C(1''')); 4.38 (*dd*, *J* =5.1, 6.6, H–C(3'')); 4.23 (*dd*, *J* = 2.6, 4.8, H–C(2'')); 4.17 (*m*, H–C(5''')); 4.08 (*t*, *J* = 1.5, H–C(3''')); 4.06 (*m*, H–C(4'')); 3.88 (*dd*, *J* = 8.8, 10.3 1H, H–C(3')); 3.77* (OC$H_{2a}$$CH_2OH$); 3.76 (*dd*, *J* =5.3, 12.5, H_a–C(5'')); 3.76* (1H, H_a–C(6')); 3.72* (H–C(5)); 3.72* (H–C(4)); 3.70* (H–C(5')); 3.68 (*d*, *J* =1.5, H–C(4''')); 3.67* (H_b–C(6')); 3.65* (OC$H_{2b}$$CH_2OH$); 3.64 (*dd*, *J* = 4.8, 12.5, H_b–C(5'')); 3.59 (*t*, J=4.4, 4.0, OCH_2CH_2OH); 3.51 (*t*, *J* = 8.8, 10.6, H–C(6)); 3.43 (*br. s*, H–C(2''')); 3.27 (*dd*, *J* = 6.6, 13.5, H_a–C(6''')); 3.27* (*dd*, *J* = 4.1, H–C(2')); 3.26* (H–C(4')); 3.23 (*dd*, *J* = 5.4, 12.2, H_b–C(6''')); 3.21* (H–C(3)); 3.15 (*dt*, *J* = 4.0, 12.5, 10.3, H–C(1)); 2.25 (*dt*, *J* = 12.8, 4.4, 4.0, H_a–C(2)); 1.78 (*s*, CH_3COOH), 1.59 (*q*, *J* = 13.2, 12.5, 12.5, H_b–C(2)). ^{13}C–NMR (150 MHz, D_2O): 181.1 (*s*, CH_3*C*OOH); 109.9 (*d*, (C1'')); 95.7 (*d*, (C1')); 95.4 (*d*, (C1''')); 84,5 (*d*, (C5)); 81.2 (*d*, (C4'')); 78.6 (*d*, (C4)); 77.7 (*d*, (C4')); 75.1 (*d*, (C3'')); 74.0 (*t*, O*C*$H_2$$CH_2OH$); 73.4 (*d*, (C2'')); 73.0 (*d*, (C5')); 72.7 (*d*, (C6)); 70.2 (*d*, (C5''')); 69.1 (*d*, (C3')); 67.7 (*d*, (C3''')); 67.3 (*d*, (C4''')); 60.9 (*t*, OCH_2*C*H_2OH); 60.1 (*t*, (C5'')); 59.9 (*t*, (C6')); 53.7 (*d*, (C2'')); 50.8 (*d*, (C2''')); 49.9 (*d*, (C1)); 48.9 (*d*, (C3)); 40.4 (*t*, (C6''')); 29.4 (*t*, (C2)), 23.0 (*q*, *C*H_3COOH). HR-ESI-Tof-MS: 660.3281 ([*M*+H]$^+$, $C_{25}H_{50}N_5O_{15}^+$; calc. 660.3303).

4'-O-*[(2,3-(*R/S*)-dihydroxy)propyl]-paromomycin* (**17**)**.** A soln. of 0.8g **27** (1eq.) in 12 mL THF and 44 mg 0.1 M aq. NaOH (2.0 eq.) was stirred for 15 min., cooled to 0°C, treated over 15 min. with 8.2 mL of a 1M soln. of PMe_3 (15 eq.), stirred for 15 min at 0° and for 18 h at r.t., and diluted with 10 mL EtOAc. Layers were separated, the aq. layer was extracted with EtOAc and the org. phases processed normally to provide 0.7 g crude that was purified by chromatography over silica (100-200 mesh, 30% EtOAc in hexanes) to provide 0.65 g (89%) of *6,3',2'',5'',3''',4'''-hexakis*-O-*(benzyl)-4'*-O-*[(2,3-(*R/S*)-dihydroxy)propyl]-paromomycin* (**29**) as pale yellow oil. A soln. of 0.6 g **29** (1.0 eq.) in 2.4 mL MeOH was added to a suspension of

0.45 g $Pd(OH)_2$ in 5.4 mL MeOH/H_2O/AcOH (4:4:1), prehydrogenated (15 bar H_2) at r.t. for 30 min. The mixture was stirred for 192 h under H_2 (25 bar). Filtration through Celite, washing with H_2O, and removal of the volatiles left 0.35 g crude that was purified by chromatography on neutralized silica gel (60-120 mesh, 10% aq. NH_3/MeOH), yielding 170 mg pale brown oil that was passed through a sephadex column followed by lyophilisation to provide 116 mg of an off-white solid that was treated with 20% aq. AcOH and lyophilized to yield 85 mg of **17** (19%). $[\alpha]_D^{24}$= +30.1 (c = 0.26, H_2O). ^{1}H-NMR (600 MHz, D_2O): 5.63 (*d*, *J* = 3.7, H–C(1')); 5.23 (*d*, *J* = 1.8, H–C(1'')); 5.15 (*d*, *J* = 1.1, H–C(1''')); 4.38 (*dd*, *J* = 5.1, 6.2, H–C(3'')); 4.24 (*dd*, *J* = 2.2, 4.8, H–C(2'')); 4.17 (*m*, H–C(5''')); 4.09 (*t*, *J* = 2.9 Hz, 3.5 Hz, H–C(3''')); 4.06 (*m*, 1H, H–C(4'')); 3.91 and 3.89 (*t*, *J*=8.8 and *t*, *J* = 8.8, 9.1, H–C(3')); 3.78* (H–C(4)); 3.77* (OCH_{2a}CH(OH)CH_2(OH)), isomer A); 3,77 (*dd*, *J* = 11.4, 4.8, 1H, H_a–C(5'')); 3.77* (H_a–C(6')); 3.76* (1H, OCH_2CH(OH)CH_2(OH)); 3.75* (H–C(5)); 3.71 (*m*, H–C(5')); 3.70* (OCH_{2a}CH(OH)CH_2(OH)), isomer B); 3.69 (*dd*, *J* = 3.8, 7.1, H–C(4''')); 3.68* (H_b–C(6')); 3.65* (OCH_{2b}CH(OH)CH_2(OH)), isomer B); 3.64 (*dd*, *J* = 11.6, 4.5, H_b–C(5'')); 3.56* (OCH_{2b}CH(OH)CH_2(OH)), isomer A); 3.54 (*t*, *J* = 9.2, 10.3, H–C(6)); 3.49 (*dd*, *J* = 10.7, 5.7, OCH_2CH(OH)CH_{2a}(OH)); 3.46 (*br. s*, H–C(2''')); 3.43 (*dd*, *J* = 10.5, 3.8, OCH_2CH(OH)CH_{2b}(OH)); 3.30* (H–C(2')); 3.29 (*dd*, *J* = 12.5, 6.1, H_a–C(6''')); 3.28* (H–C(3)); 3.27* (H–C(4')); 3.24 (*dd*, *J* = 12.5, 4.8 Hz, H_b–C(6''')); 3.18 (*dt*, *J* = 4.0, 12.5, 11.0, H–C(1)); 2.25 (*dt*, *J* = 12.8, 4.3, 4.0, H_a–C(2)); 1.77 (*s*, CH_3COOH); 1.64 (*q*, *J* =10.3, 12.8, 12.8, 1H, H_b–C(2)). ^{13}C–NMR (150 MHz, D_2O): 180.8 (*s*, CH_3*C*OOH; 110.0 (*d*, (C1'')); 95.6 (*d*, (C1')); 95.3 (*d*, (C1''')); 84.4 (*d*, (C5)); 81.2 (*d*, (C4'')); 78.1 (*d*, (C4)); 77.9 and 77.8* (*d*, (C4')); 75.1 (*d*, (C3'')); 73.9 (*t*, O*C*H_2CH(OH)CH_2(OH), isomer A); 73.7 (*t*, O*C*H_2CH(OH)CH_2(OH), isomer B); 73.3 (*d*, (C2'')); 73.0 and 73.0* (*d*, (C5')); 72.5 (*d*, (C6)); 70.8 and 70.4 (*d*, OCH_2*C*H(OH)CH_2(OH); isomer A and B); 70.2 (*d*, (C5''')); 69.0 (*d*, (C3')); 67.6 (*d*, (C3''')); 67.2 (*d*, (C4''')); 62.3 (*t*, O*C*H_2CH(OH)CH_2(OH)); 60.0 (*t*, (C5'')); 59.9 (t, (C6')); 53.7 (*d*, (C2')), 50.8 (*d*, (C2''')), 49.9 (*d*, (C1)), 48.8 (*d*, (C3)), 40.4 (*t*, (C6''')), 28.9 (*t*,

(C2)), 22.9 (*q*, *C*H_3COOH). HR-ESI-Tof-MS: 712.3217 ([*M*+H]$^+$, $C_{25}H_{50}N_5O_{15}^+$; calc. 712.3229).

6,3',2",5",3"',4"'-Hexa-O-*acetyl-1,3,2',2"',6"'-pentazido-1,3,2',2"',6"'-pentadeamino-6'*-O-*pivaloylparomomycin* (**31**). A soln. of **30** [2] (500 mg, 0.5 mmol) in dry pyridine (5 mL) was treated with pivaloyl chloride (123 µl, 1 mmol) and a catalytic amount of DMAP (6.1 mg, 0.05 mmol), stirred at 26 °C for 10 h, and evaporated. FC (pentane/EtOAc 6:4) gave **31** (390 mg, 72%) as white powder. R_f (pentane/EtOAc 1:1) 0.60. IR (ATR): 2938*w*, 2104*s*, 1739*m*, 1615*m*, 1515*m*, 1240*s*, 1035*s*. ^{1}H-NMR (600 MHz, $CDCl_3$): 5.90 (*d*, *J* = 3.8, H–C(1')); 5.35 (*d*, *J* = 2.8, H–C(1'')); 5.33 (*dd*, *J* = 10.8, 9.2, H–C(3')); 5.03 (*t*, *J* = 2.8, H–C(3''')); 4.92 (*dd*, *J* = 10.0, 9.4, H–C(6)); 4.874 (*dd*, *J* = 5.6, 2.9, H–C(2'')); 4.870 (*d*, *J* = 2.2, H–C(1''')); 4.70 (*ddd*, *J* = 2.8, 1.9, 0.8, H–C(4''')); 4.46 (*dd*, *J* = 12.2, 4.3, H_a–C(6')); 4.43 (*dd*, *J* = 12.2, 2.3, H_a–C(5'')); 4.41 (*dd*, *J* = 6.2, 5.2, H–C(3'')); 4.32 (*ddd*, *J* = 6.2, 4.6, 2.4, H–C(4'')); 4.28 (*dd*, *J* = 12.2, 2.2, H_b–C(6')); 4.24 (*ddd*, *J* = 9.8, 4.2, 2.4, H–C(5')); 4.23 (*dd*, *J* = 12.2, 4.6, H_b–C(5'')); 4.09 (*ddd*, *J* = 8.2, 4.3, 1.9, H–C(5''')); 3.89 (*dd*, *J* = 9.2, 8.8, H–C(5)); 3.68 (*dd*, *J* = 9.7, 8.7, H–C(4)); 3.59 (*dd*, *J* = 13.0, 8.2, H_a–C(6''')); 3.52 (*ddd*, *J* = 12.4, 9.8, 4.6, H–C(3)); 3.45–3.39 (*m*, H–C(1), H–C(4')); 3.32 (*ddd*, *J* = 2.8, 1.9, 0.8, H–C(2''')); 3.27 (*dd*, *J* = 13.0, 4.3, H_b–C(6''')); 3.03 (*dd*, *J* = 10.7, 3.7, H–C(2')); 2.99 (br. *s*, HO–C(4')); 2.35 (*dt*, *J* = 13.3, 4.5, H_{eq}–C(2)); 2.18, 2.17, 2.164, 2.156, 2.12, 2.09 (6*s*, 6 OAc); 1.53 (*q*, *J* = 12.7, H_{ax}–C(2)); 1.24 (*s*, CMe_3). ^{13}C-NMR (150 MHZ, $CDCl_3$): 179.2 (*s*, Me_3C–*C*=O); 171.4, 170.8, 170.3, 169.9, 169.7, 168.6 (6*s*, 6 Me*C*=O); 107.2 (*d*, C(1'')); 99.4 (*d*, C(1''')); 96.6 (*d*, C(1')); 82.4 (*d*, C(5)); 79.7 (*d*, C(4'')); 76.1 (*d*, C(3'')); 75.9 (*d*, C(4)); 75.5 (*d*, C(2'')); 75.1 (*d*, C(6)); 73.6 (*d*, C(5''')); 72.7 (*d*, C(3')); 71.1 (*d*, C(5')); 69.9 (*d*, C(4')); 68.8 (*d*, (3''')); 65.8 (*d*, C(4''')); 63.5 (*t*, C(6')); 63.1 (*t*, C(5'')); 60.9 (*d*, C(2')); 59.4 (*d*, C(3)); 58.2 (*d*, C(1)); 56.7 (*d*, C(2''')); 50.8 (*t*, C(6''')); 39.1 (*s*, *C*Me_3); 31.8 (*t*, C(2)); 27.4 (*q*, C*Me*$_3$); 20.88, 20.85, 20.73, 20.71, 20.64, 20.5 (6*q*, 6 *Me*C=O). HR-MALDI-MS: 1104.3562 (100, [*M* + Na]$^+$, $C_{40}H_{55}N_{15}NaO_{21}^+$; calc. 1104.3589).

6,3',2'',5'',3''',4'''-Hexa-O-*acetyl-1,3,2',2''',6'''-pentazido-1,3,2',2''',6'''-pentadeamino-4'*-O-*(methoxymethyl)-6'*-O-*pivaloylparomomycin* (**32**). A soln. of **31** (100 mg, 92 μmol) in dimethoxymethane (5 mL) under N_2 at 0 °C was treated with $FeCl_3$ (3 mg, 0.2 eq.), and stirred at 26 °C for 10 h. The mixture was basified with 1 M NaOH (pH > 7), and extracted with EtOAc (3 x). The combined organic phases were washed with water and brine, dried ($MgSO_4$,), filtered, and evaporated. FC (pentane/EtOAc 7:3) gave **32** (107 mg, 97%) as colorless viscous oil. R_f (pentane/EtOAc 6:4) 0.58. $[\alpha]_D^{23}$ = +65.6 (*c* = 0.2, $CHCl_3$). IR (ATR): 2910*w*, 2837*w*, 2101*s*, 1743*s*, 1450*w*, 1376*w*, 1371*m*, 1217*s*, 1158*m*, 1035*s*. ^{1}H-NMR (600 MHz, $CDCl_3$): 5.89 (*d*, *J* = 3.7, H–C(1')); 5.47 (*dd*, *J* = 10.8, 9.0, H–C(3')); 5.35 (*d*, *J* = 3.1, H–C(1'')); 5.02 (*t*, *J* = 2.9, H–C(3''')); 4.91 (*dd*, *J* = 10.0, 9.5, H–C(6)); 4.865 (*d*, *J* = 2.2, H–C(1''')); 4.864 (*t*, *J* ≈ 4.0, H–C(2'')); 4.70 (*d*, *J* = 6.9, OCH_aO); 4.69 (*td*, *J* = 2.6, 0.8, H–C(4''')); 4.58 (*d*, *J* = 6.9, OCH_bO); 4.43 (*dd*, *J* = 12.2, 2.4, H_a–C(5'')); 4.40 (*dd*, *J* = 6.2, 5.3, H–C(3'')); 4.36 (*ddd*, *J* = 10.0, 4.1, 1.9, H–C(5')); 4.345 (*dd*, *J* = 12.3, 1.9, H_a–C(6')); 4.32 (*ddd*, *J* = 6.2, 4.7, 2.4, H–C(4'')); 4.234 (*dd*, *J* = 12.3, 4.7, H_b–C(6')); 4.226 (*dd*, *J* = 12.3, 4.6, H_b–C(5'')); 4.08 (*ddd*, *J* = 8.2, 4.3, 1.9, H–C(5''')); 3.89 (*t*, *J* ≈ 9.2, H–C(5)); 3.66 (*dd*, *J* = 9.8, 8.8, H–C(4)); 3.60 (*dd*, *J* = 10.0, 9.2, H–C(4')); 3.57 (*dd*, *J* = 13.0, 8.2, H_a–C(6''')); 3.51 (*ddd*, *J* = 12.5, 9.8, 4.6, H–C(3)); 3.41 (*ddd*, *J* = 12.5, 10.1, 4.4, H–C(1)); 3.33 (*s*, OMe); 3.32 (*td*, *J* = 2.8, 0.8, H–C(2''')); 3.26 (*dd*, *J* = 13.0, 4.3, H_b–C(6''')); 2.90 (*dd*, *J* = 10.8, 3.7, H–C(2')); 2.36 (*dt*, *J* = 13.3, 4.5, H_{eq}–C(2)); 2.17, 2.16, 2.155, 2.15, 2.12, 2.08 (6*s*, 6 OAc); 1.54 (*q*, *J* = 13.1, H_{ax}–C(2)); 1.23 (s, CMe_3). ^{13}C-NMR (150 MHz, $CDCl_3$): 178.1 (*s*, Me_3C–*C*=O); 170.7, 170.1, 170.0, 169.8, 169.6, 168.5 (6*s*, 6 Me*C*=O); 107.0 (*d*, C(1'')); 99.3 (*d*, C(1''')); 97.9 (OCH_2O), 96.6 (*d*, C(1')); 82.3 (*d*, C(5)); 79.6 (*d*, C(4'')); 76.0 (*d*, C(3'')); 75.7 (*d*, C(4)); 75.40 (*d*, C(6)); 75.37 (*d*, C(4')); 75.0 (*d*, C(2'')); 73.4 (*d*, C(5''')); 71.5 (*d*, C(3')); 69.3 (*d*, C(5')); 68.7 (*d*, C(3''')); 65.7 (*d*, C(4''')); 63.4 (*t*, C(5'')); 62.6 (*t*, C(6')); 61.0 (*d*, C(2')); 59.3 (*d*, C(3)); 58.1 (*d*, C(1)); 56.6 (*q*, OMe); 56.4 (*d*, C(2''')); 50.6 (*t*, C(6''')); 38.9 (s *C*Me_3); 31.7 (*t*, C(2)); 27.2 (*q*, C*Me*$_3$); 21.0, 20.9, 20.8, 20.75, 20.7, 20.5

(6*q*, 6 *Me*C=O). HR-MALDI-MS: 1148.3839 (100, $[M + Na]^+$, $C_{42}H_{59}N_{15}NaO_{22}^+$; calc. 1148.3851).

4'-O-*(Methoxymethyl)paromomycin* (**18**) *and its Acetate* **18**·0.15 AcOH. A soln. of **32** (300 mg, 0.27 mmol) in 0.1 M MeONa in MeOH (10 mL) was stirred at 26 °C for 6 h, neutralized with Amberlite-IR 120 (H^+ form), filtered, and evaporated. A soln. of the residue (150 mg) in THF (3 mL) was treated with 0.1 N NaOH (2.8 mL, 0.28 mmol) and 1 M PMe_3 in THF (1.12 mL, 1.12 mmol.), stirred at 60 °C for 8 h, and evaporated. FC (MeOH/25% aq. NH_3 4:1) gave **18** (105 mg, 83%) as a colorless powder. R_f (MeOH/25% aq. NH_3 4:1) 0.26. IR (ATR): 3210*m*, 2980*m*, 1565*m*, 1403*m*, 1397*m*, 1108*s*, 970*m*. Dissolution of **18** in AcOH/H_2O 1:1, partial evaporation, and lyophilization gave **18**·0.15 AcOH as a colorless powder. ^{1}H-NMR (500 MHz, D_2O): 5.83 (*d*, *J* = 3.9, H–C(1')); 5.42 (*d*, *J* = 2.2, H–C(1'')); 5.33 (*d*, *J* = 1.6, H–C(1''')); 4.90 and 4.81 (2*d*, *J* = 6.9, OC*H*$_2$OMe); 4.58 (*dd*, *J* = 6.8, 4.9, H–C(3'')); 4.45 (*dd*, *J* = 4.8, 2.3, H–C(2'')); 4.36 (*ddd*, *J* = 7.0, 4.0, 1.5, H–C(5''')); 4.28 (*t*, *J* = 3.1, H–C(3''')); 4.26–4.22 (*m*, H–C(4'')); 4.08 (*dd*, *J* = 10.6, 8.9, H–C(3')); 4.07 (*t*, *J* = 9.8, H–C(4)); 3.98–3.91 (*m*, H–C(5), H_a–C(6'), H_a–C(5'')); 3.92–3.87 (*m*, H–C(5')); 3.85 (*dd*, *J* = 3.2, 1.5, H–C(4''')); 3.82–3.75 (*m*, H–C(6), H_b–C(6'), H_b–C(5'')); 3.63–3.55 (*m*, H–C(3), H–C(4'), H–C(2''')); 3.49 (*dd*, *J* = 10.6, 3.9, H–C(2')); 3.49–3.36 (*m*, H–C(1), H_2C(6''')); 3.47 (*s*, OMe); 2.51 (*dt*, *J* = 12.6, 4.3, H_{eq}–C(2)); 1.93 (*s*, 0.15 MeCO_2^-); 1.92 (*q*, *J* = 12.6, H_{ax}–C(2)). ^{13}C-NMR (125 MHz, D_2O): 181.0 (*s*, Me*C*O_2^-); 110.0 (*d*, C(1'')); 97.6 (*t*, O*C*H$_2$OMe); 95.7 (*d*, C(1')); 95.1 (*d*, C(1''')); 84.2 (*d*, C(5)); 81.2 (*d*, C(4'')); 77.7 (*d*, C(4)); 75.8 (*d*, C(4')); 74.8 (*d*, C(3'')); 73.1 (*d*, C(2'')); 72.8 (*d*, C(5')); 72.2 (*d*, C(6)); 70.3 (*d*, C(5''')); 68.6 (*d*, C(3')); 67.7 (*d*, C(3''')); 67.1 (*d*, C(4''')); 60.1 and 59.9 (2*t*, C(6'), C(5'')); 56.1 (*q*, OMe); 53.7 (*d*, C(2')); 50.8 (*d*, C(2''')); 49.8 (*d*, C(1)); 48.8 (*d*, C(3)); 40.3 (*t*, C(6''')); 28.3 (*t*, C(2)); 23.0 (*q*, *Me*CO_2^-). HR-MALDI-MS: 660.3289 (100, $[M + H]^+$, $C_{25}H_{50}N_5O_{15}^+$; calc. 660.3298).

6,3',2'',5'',3''',4'''-Hexa-O-*acetyl-1,3,2',2''',6'''-pentazido-1,3,2',2''',6'''-pentadeamino-6'*-O-*(methoxymethyl)paromomycin* (**33**). A soln. of **30** (300 mg, 0.3 mmol) in dimethoxymethane

(5 mL) at 0 °C was treated with a catalytic amount of anhydrous $FeCl_3$ (13 mg, 0.08 mmol), and stirred for 6 h. The mixture was basified with 1 N NaOH (pH > 7) and extracted with EtOAc (3 x 25 mL). The combined organic phases were washed with water and brine, dried ($MgSO_4$), filtered, and evaporated. FC (pentane/EtOAc 7:3) gave **33** (256 mg, 82%) as colorless oil. R_f (pentane/EtOAc 6:4) 0.45. IR (ATR): 2938*w*, 2101*s*, 1739*s*, 1614*m*, 1371*s*, 1211*s*, 1147*m*. ^{1}H-NMR (600 MHz, $CDCl_3$): 5.90 (*d*, *J* = 3.7, H–C(1')); 5.35 (*d*, *J* = 2.6, H–C(1'')); 5.33 (*dd*, *J* = 10.6, 9.2, H–C(3')); 5.03 (*t*, *J* = 2.8, H–C(3''')); 4.94 (*dd*, *J* = 10.0, 9.4, H–C(6)); 4.87 (*dd*, *J* = 5.1, 2.8, H–C(2'')); 4.86 (*d*, *J* = 1.9, H–C(1''')); 4.70 (*ddd*, *J* = 2.7, 2.0. 0.7, H–C(4''')); 4.67 and 4.65 (2*d*, *J* = 6.4, OCH_2O); 4.41 (*dd*, *J* = 12.1, 2.4, H_a–C(5'')); 4.38 (*dd*, *J* = 6.4, 5.2, H–C(3'')); 4.31 (*ddd*, *J* = 6.0, 4.8, 2.4, H–C(4'')); 4.24 (*dd*, *J* = 12.1, 5.0, H_b–C(5'')); 4.17 *(dt*, *J* ≈ 9.9, 3.6, H–C(5')); 4.08 (*ddd*, *J* = 8.0, 4.5, 1.9, H–C(5''')); 3.89 (*t*, *J* = 8.9, H–C(5)); 3.85 (*dd*, *J* = 11.0, 3.9, H_a–C(6')); 3.77 (*dd*, *J* = 11.0, 3.3, H_b–C(6')); 3.74–3.70 (*m*, H–C(4')); 3.71 (*dd*, *J* = 9.6, 8.6, H–C(4)); 3.59 (*dd*, *J* = 13.0, 8.0, H_a–C(6''')); 3.49 (*ddd*, *J* = 12.5, 9.7, 4.6, H–C(3)); 3.42 (*ddd*, *J* = 12.4, 10.1, 4.5, H–C(1)); 3.38 (*s*, OMe); 3.32 (*ddd*, *J* = 2.8, 2.0, 0.7, H–C(2''')); 3.29 (*dd*, *J* = 13.0, 4.5, H_b–C(6''')); 3.09 (*dd*, *J* = 10.7, 3.7, H–C(2')); 2.78 (br. s, HO–C(4')); 2.35 *(dt*, *J* = 13.3, 4.5, H_{eq}–C(2)); 2.18, 2.17, 2.164, 2.159, 2.12, 2.10 (6*s*, 6 OAc); 1.58 (*q*, *J* = 12.8, H_{ax}–C(2)). ^{13}C-NMR (150 MHz, $CDCl_3$): 171.5, 170.8, 170.1, 169.8, 169.6, 168.5 (6*s*, 6 Me*C*=O); 106.9 (*d*, C(1'')); 99.3 (*d*, C(1''')); 96.8 (*t*, OCH_2O); 96.6 (*d*, C(1')); 82.0 (*d*, C(5)); 79.5 (*d*, C(4'')); 76.0 (*d*, C(4)); 75.9 (*d*, C(3'')); 75.4 (*d*, C(6)); 74.9 (*d*, C(2'')); 73.4 (*d*, C(5''')); 73.1 (*d*, C(3')); 71.1 (*d*, C(5')); 69.8 (*d*, C(4')); 68.7 (*d*, C(3''')); 66.6 (*t*, C(6')); 65.7 (*d*, C(4''')); 63.6 (*t*, C(5'')); 60.7 (*d*, C(2')); 59.3 (*d*, C(3)); 58.1 (*d*, C(1)); 56.6 (*d*, C(2''')); 55.4 (*q*, OMe); 50.6 (*t*, C(6''')); 31.5 (*t*, C(2)); 20.95, 20.90, 20.79, 20.74, 20.68, 20.54 (6*q*, 6 *Me*C=O). HR-MALDI-MS: 1064.3308 (100, $[M + Na]^+$, $C_{37}H_{51}N_{15}NaO_{21}^+$; calc. 1064.3276).

6'-O-(Methoxymethyl)paromomycin (**19**) *and its Diacetate* **19**·2 AcOH. A soln. of **33** (300 mg, 0.27 mmol) in 0.1 M MeONa in MeOH (10 mL) was stirred at 26 °C for 6 h, acidified with *Amberlite-IR 120* (H^+ form), filtered, and evaporated. A soln. of the residue (149 mg) in THF (3

mL) was treated with 0.1 N NaOH (2.8 mL, 0.28 mmol) and 1 M PMe_3 in THF (1.12 mL, 1.12 mmol), stirred at 60 °C for 5 h, and evaporated. FC (MeOH/25% aq. NH_3 4:1) gave **19** (99 mg, 82%) as colorless powder. R_f (MeOH/25% aq. NH_3 4:1) 0.25. IR (ATR): 3211*m*, 2940*m*, 1565*m*, 1403*m*, 1397*m*, 1108*s*, 970*m*. Dissolution of **19** in AcOH/H_2O 1:1, partial evaporation, and lyophilization gave **19**·2 AcOH as colorless powder. $[\alpha]_D^{23}$ = +51.5 (*c* = 0.5, H_2O). ^{1}H-NMR (500 MHz, D_2O): 5.76 (*d*, *J* = 4.0, H–C(1')); 5.37 (*d*, *J* = 2.4, H–C(1'')); 5.28 (*d*, *J* = 1.7, H–C(1''')); 4.70 and 4.67 (2*d*, *J* = 6.8, OCH_2OMe); 4.51 (*dd*, *J* = 6.8, 4.9, H–C(3'')); 4.40 (*dd*, *J* = 4.8, 2.4, H–C(2'')); 4.31 (*ddd*, *J* = 7.0, 4.0, 1.5, H–C(5''')); 4.22 (*t*, *J* = 3.2, H–C(3''')); 4.19 (*ddd*, *J* = 6.7, 4.7, 3.1, H–C(4'')); 4.02 (*dd*, *J* = 10.1, 9.1, H–C(4)); 3.93 (*dd*, *J* = 10.8, 9.1, H–C(3')); 3.92 (*t*, *J* = 9.1, H–C(5)); 3.92–3.86 (*m*, H–C(5'), H_a–C(6'), H_a–C(5'')); 3.79 (*dt*, *J* = 3.1, 1.4, H–C(4''')); 3.78–3.71 (*m*, H–C(6), H_b–C(6'), H_b–C(5'')); 3.60–3.54 (*m*, H–C(3)); 3.57 (*dt*, *J* = 3.3, 1.4, H–C(2''')); 3.50 (*t*, *J* = 9.4, H–C(4')); 3.40 (*dd*, *J* = 10.8, 4.0, H–C(2')); 3.36 (*s*, OMe); 3.41–3.31 (*m*, H–C(1), H_2C(6''')); 2.49 (*dt*, *J* = 12.6, 4.2, H_{eq}–C(2)); 1.94 (*s*, 2 $MeCO_2^-$); 1.89 (*q*, *J* = 12.6, H_{ax}–C(2)). ^{13}C-NMR (125 MHz, D_2O): 178.6 (*s*, Me*C*O_2^-); 109.8 (*d*, C(1'')); 96.02 (*t*, O*C*H_2OMe); 95.96 (*d*, C(1')); 94.9 (*d*, C(1''')); 83.9 (*d*, C(5)); 81.0 (*d*, C(4'')); 77.5 (*d*, C(4)); 74.6 (*d*, C(3'')); 73.0 (*d*, C(2'')); 72.2 (*d*, C(5')); 72.0 (*d*, C(6)); 70.1 (*d*, C(5''')); 69.0 (*d*, C(4')); 68.6 (*d*, C(3')); 67.4 (*d*, C(3''')); 66.9 (*d*, C(4''')); 66.0 (*t*, C(6')); 59.8 (*t*, C(5'')); 54.9 (*q*, OMe); 53.6 (*d*, C(2')); 50.6 (*d*, C(2''')); 49.6 (*d*, C(1)); 48.6 (*d*, C(3)); 40.1 (*t*, C(6''')); 27.8 (*t*, C(2)); 21.4 (*q*, *Me*CO_2^-). HR-MALDI-MS: 660.3296 (100, $[M + H]^+$, $C_{25}H_{50}N_5O_{15}^+$; calc. 660.3298).

6,3',2'',5'',3''',4'''-Hexa-O-*acetyl-1,3,2',2''',6'''-pentazido-1,3,2',2''',6'''-pentadeamino-4',6'-bis*-O-*(methoxymethyl)paromomycin* (**24**). A soln. of **30** (402 mg, 0.4 mmol) in dimethoxymethane (20 mL) under N_2 at 0 °C was treated with $FeCl_3$ (13 mg, 0.08 mmol), and stirred at 26 °C for 10 h. The mixture was basified with 1 M NaOH (pH > 7), and extracted with EtOAc (3 x). The combined organic phases were washed with water and brine, dried ($MgSO_4$), filtered, and evaporated. FC (pentane/EtOAc 7:3) gave **34** (349 mg, 80%) as colorless viscous

oil. R_f (pentane/EtOAc 6:4) 0.57. $[\alpha]_D^{23}$ = +73.8 (*c* = 0.63, $CHCl_3$). IR (ATR): 2934*w*, 2100*s*, 1741*s*, 1439*w*, 1371*m*, 1215*s*, 1147*m*, 1037*s*, 915*m*. ^{1}H-NMR (600 MHz, $CDCl_3$): 5.88 (*d*, *J* = 3.8, H–C(1')); 5.47 (*dd*, *J* = 10.8, 9.1, H–C(3')); 5.34 (*d*, *J* = 2.8, H–C(1'')); 5.02 (*t*, *J* = 2.8, H–C(3''')); 4.93 (*dd*, *J* = 10.0, 9.3, H–C(6)); 4.86 (*dd*, *J* = 5.1, 2.8, H–C(2'')); 4.85 (*d*, *J* = 1.9, H–C(1''')); 4.69 (*ddd*, *J* = 2.8, 2.0, 0.8, H–C(4''')); 4.68 (br. *s*, OCH_2O); 4.67 and 4.63 (2*d*, *J* = 6.5, OCH_2O); 4.39 (*dd*, *J* = 12.2, 2.5, H_a–C(5'')); 4.37 (*dd*, *J* = 6.3, 5.1, H–C(3'')); 4.30 (*ddd*, *J* = 6.5, 4.9, 2.3, H–C(4'')); 4.24–4.21 (*m*, H–C(5')); 4.23 (*dd*, *J* = 12.2, 4.8, H_b–C(5'')); 4.07 (*ddd*, *J* = 8.0, 4.7, 1.9, H–C(5''')); 3.89 (*dd*, *J* = 9.3, 8.8, H–C(5)); 3.76 (*d*, *J* = 2.8, H_2C(6')); 3.705 (*dd*, *J* = 9.8, 9.2, H–C(4')); 3.699 (*dd*, *J* = 9.6, 8.7, H–C(4)); 3.58 (*dd*, *J* = 13.0, 8.0, H_a–C(6''')); 3.48 (*ddd*, *J* = 12.5, 9.7, 4.6, H–C(3)); 3.43 (*ddd*, *J* = 12.5, 10.0, 4.5, H–C(1)); 3.37, 3.34 (2*s*, 2 OMe); 3.31 (*td*, *J* ≈ 2.4, 0.8, H–C(2''')); 3.28 (*dd*, *J* = 13.0, 4.6, H_b–C(6''')); 2.94 (*dd*, *J* = 10.8, 3.8, H–C(2')); 2.35 (*dt*, *J* = 13.3, 4.5, H_{eq}–C(2)); 2.17, 2.16, 2.158, 2.14, 2.11, 2.10 (6*s*, 6 OAc); 1.57 (*q*, *J* = 12.8, H_{ax}–C(2)). ^{13}C-NMR (150 MHz, $CDCl_3$): 170.8, 170.14, 170.12, 169.8, 169.6, 168.5 (6*s*, 6 Me*C*=O); 106.8 (*d*, C(1'')); 99.3 (*d*, C(1''')); 97.9, 96.9 (2*t*, 2 OCH_2O); 96.8 (*d*, C(1')); 82.0 (*d*, C(5)); 79.4 (*d*, C(4'')); 76.0 (*d*, C(3'')); 75.9 (*d*, C(4)); 75.5 *d*, C(4')); 75.4 (*d*, C(6)); 74.9 (*d*, C(2'')); 73.4 (*d*, C(5''')); 71.5 (*d*, C(3')); 70.6 (*d*, C(5')); 68.7 (*d*, C(3''')); 65.8 (*t*, C(6')); 65.7 (*d*, C(4''')); 63.6 (*t*, C(5'')); 61.1 (*d*, C(2')); 59.3 (*d*, C(3)); 58.1 (*d*, C(1)); 56.6 (*d*, C(2''')); 56.3, 55.4 (2*q*, 2 OMe); 50.6 (*t*, C(6''')); 31.5 (*t*, C(2)); 21.0, 20.9, 20.8, 20.69, 20.67, 20.5 (6*q*, 6 *Me*C=O). HR-MALDI-MS: 1108.3541 (100, $[M + Na]^+$, $C_{39}H_{55}N_{15}NaO_{22}^+$; calc. 1108.3538).

4',6'-Bis-O-*(methoxymethyl)paromomycin* (**20**) *and its Diacetate* **20**·2 AcOH. A soln. of **34** (328 mg, 0.29 mmol) in 0.1 M MeONa in MeOH (20 mL) under N_2 was stirred at 26 °C for 2 h, acidified with *Amberlite IR-120* (H^+ form), filtered, and evaporated A soln. of the residue (212 mg) in THF (2 mL) was treated with 0.1 N NaOH (3.8 mL, 0.38 mmol) and 1 M PMe_3 in THF (1.5 mL, 1.52 mmol.), stirred at 60 °C for 8 h, and evaporated. FC (MeOH/25% aq. NH_3 4:1) gave **20** (171 mg, 84%) as a white powder. R_f (MeOH/25% aq. NH_3 4:1) 0.26. IR (ATR): 3210*m*,

2980*m*, 1565*m*, 1403*m*, 1397*m*, 1108*s*, 970*m*. Dissolution of **20** in AcOH/H_2O 1:1, partial evaporation, and lyophilization gave the **20**·2 AcOH as white powder. $[\alpha]_D^{23}$ = +36.1 (*c* = 0.54, H_2O). ^{1}H-NMR (600 MHz, D_2O): 5.81 (*d*, *J* = 4.0, H–C(1')); 5.43 (*d*, *J* = 2.2, H–C(1'')); 5.34 (*d*, *J* = 1.6, H–C(1''')); 4.91 and 4.83 (2*d*, *J* = 7.0, OC*H*$_2$OMe); 4.78 and 4.75 (2*d*, *J* = 6.8, OC*H*$_2$OMe); 4.58 (*dd*, *J* = 6.8, 4.9, H–C(3'')); 4.46 (*dd*, *J* = 4.8, 2.3, H–C(2'')); 4.37 (*ddd*, *J* = 6.8, 3.9, 1.4, H–C(5''')); 4.29 (*t*, *J* = 3.1, H–C(3''')); 4.26 (*ddd*, *J* = 6.7, 4.6, 3.2, H–C(4'')); 4.10 (*dd*, *J* = 10.6, 8.9, H–C(3')); 4.05 (*dd*, *J* = 9.8, 9.3, H–C(4)); 4.04 (*ddd*, *J* = 9.4, 5.9, 2.2, H–C(5')); 3.97 (*t*, *J* = 9.1, H–C(5)); 3.95 (br. *dd*, *J* ≈ 11.6, 2.2, H_a–C(6'), H_a–C(5'')); 3.87–3.86 (*m*, H–C(4''')); 3.84 (*dd*, *J* = 11.2, 5.8, H_b–C(6')); 3.80 (*dd*, *J* = 12.4, 4.8, H_b–C(5'')); 3.79 (*dd*, *J* = 10.7, 9.5, H–C(6)); 3.65 (*t*, *J* = 9.2, H–C(4')); 3.64 (*dt*, *J* = 3.0, 1.2, H_b–C(2''')); 3.60 (*ddd*, *J* = 12.7, 10.1, 4.1, H–C(3)); 3.50 (*dd*, *J* = 10.6, 4.0, H–C(2')); 3.48 (*s*, OMe); 3.46 (*dd*, *J* = 13.3, 7.0, H_a–C(6''')); 3.44 (*s*, OMe); 3.43–3.37 (m, H–C(1)); 3.42 (*dd*, *J* = 13.5, 3.8, H_b–C(6''')); 2.54 (*dt*, *J* = 12.7, 4.2, H_{eq}–C(2)); 1.95 (*s*, 2 $MeCO_2^-$); 1.91 (*q*, *J* = 12.7, H_{ax}–C(2)). ^{13}C-NMR (150 MHz, D_2O): 180.8 (*s*, Me*C*O_2^-); 110.0 (*d*, C(1'')); 97.6, 96.3 (2*t*, 2 O*C*H_2OMe); 95.8 (*d*, C(1')); 95.2 (*d*, C(1''')); 84.1 (*d*, C(5)); 81.2 (*d*, C(4'')); 78.0 (*d*, C(4)); 75.9 (*d*, C(4')); 74.9 (*d*, C(3'')); 73.2 (*d*, C(2'')); 72.3 (*d*, C(6)); 71.5 (*d*, C(5')); 70.3 (*d*, C(5''')); 68.5 (*d*, C(3')); 67.6 (*d*, C(3''')); 67.2 (*d*, C(4''')); 66.0 (*t*, C(6')); 60.1 (*t*, C(5'')); 56.1, 55.3 (2*q*, 2 OMe); 53.6 (*d*, C(2')); 50.8 (*d*, C(2''')); 49.8 (*d*, C(1)); 48.8 (*d*, C(3)); 40.4 (*t*, C(6''')); 28.2 (*t*, C(2)); 22.9 (*q*, *Me*CO_2^-). HR-MALDI-MS: 726.3385 (100, $[M + Na]^+$, $C_{27}H_{55}N_5NaO_{16}^+$; calc. 726.3380).

6,3',2'',5'',3''',4'''-Hexa-O-*acetyl-1,3,2',2''',6'''-pentazido-1,3,2',2''',6'''-pentadeamino-4',6'*-O-*methyleneparomomycin* (**35**). A soln. of DMSO (107 mg, 1.5 mmol) in dry toluene (3 mL) at 0 °C was treated with trimethyl chlorosilane (TMSCl; 190 mg, 1.5 mmol), stirred at 26 °C for 2 h until a white precipitate appeared. Toluene was removed by decanting, and the white precipitate was quickly rinsed with CH_2Cl_2 (1 mL). A soln. of **30** (500 mg, 0.5 mmol) in CH_2Cl_2 (5 mL) was added to this precipitate. The mixture was heated to reflux for 6 h, cooled to r.t., washed with 10% aqueous $NaHCO_3$ and water, dried ($MgSO_4$), filtered, and evaporated. FC

(pentane/EtOAc 7:3) gave **35** (227 mg, 45%) as colorless oil. R_f (pentane/EtOAc 7:3) 0.43. $[\alpha]_D^{23}$ = +50.9 (*c* = 0.5, $CHCl_3$). IR (ATR): 2928*w*, 2099*s*, 1739*s*, 1615*w*, 1371*s*, 1211*s*, 1147*m*. ^{1}H-NMR (600 MHz, $CDCl_3$): 5.82 (*d*, *J* = 3.9, H–C(1')); 5.50 (*dd*, *J* = 10.3, 9.7, H–C(3')); 5.34 (*d*, *J* = 2.5, H–C(1'')); 5.05 (*d*, *J* = 6.2, $OCH_{eq}O$); 5.03 (*t*, *J* = 2.8, H–C(3''')); 4.93 (*dd*, *J* = 10.0, 9.3, H–C(6)); 4.90 (*dd*, *J* = 4.9, 2.4, H–C(2'')); 4.88 (*d*, *J* = 1.8, H–C(1''')); 4.70 (*ddd*, *J* = 2.7, 1.9, 0.8, H–C(4''')); 4.57 (*d*, *J* = 6.3, $OCH_{ax}O$); 4.42 (*dd*, *J* = 12.3, 2.6, H_a–C(5'')); 4.40 (*dd*, *J* = 6.7, 5.0, H–C(3'')); 4.30 (*ddd*, *J* = 6.7, 5.1, 2.3, H–C(4'')); 4.21 (*dd*, *J* = 12.2, 5.1, H_b–C(5'')); 4.20–4.15 (*m*, H–C(5'), H_{eq}–C(6')); 4.10 (*ddd*, *J* = 8.2, 4.1, 1.9, H–C(5''')); 3.88 (*dd*, *J* = 9.1, 8.6, H–C(5)); 3.65 (*dd*, *J* = 9.7, 8.5, H–C(4)); 3.59 (*dd*, *J* = 13.0, 8.2, H_a–C(6''')); 3.49 (*ddd*, *J* = 12.5, 9.7, 4.6, H–C(3)); 3.45–3.40 (*m*, H–C(1), H_{ax}–C(6')); 3.325 (*t*, *J* = 9.6, H–C(4')); 3.315 (*ddd*, *J* = 2.8, 2.0, 0.7w, H–C(2''')); 3.25 (*dd*, *J* = 13.0, 4.1, H_b–C(6''')); 3.07 (*dd*, *J* = 10.4, 3.9, H–C(2')); 2.38 (*dt*, *J* = 13.3, 4.6, H_{eq}–C(2)); 2.172, 2.167, 2.156, 2.147, 2.114, 2.085 (6*s*, 6 OAc); 1.59 (*q*, *J* = 12.6, H_{ax}–C(2)). ^{13}C-NMR (150 MHz, $CDCl_3$): 170.7, 170.13, 170.06, 169.8, 169.7, 168.5 (6*s*, 6 Me*C*=O); 107.1 (*d*, C(1'')); 99.1 (*d*, C(1''')); 97.4 (*d*, C(1')); 93.7 (*t*, OCH_2O); 82.2 (*d*, C(5)); 79.3 (*d*, C(4'')); 79.1 (*d*, C(4')); 76.4 (*d*, C(4)); 75.8 (*d*, C(3'')); 75.3 (*d*, C(6)); 74.8 (*d*, C(2'')); 73.6 (*d*, C(5''')); 69.0 (*d*, C(3')); 68.7 (*d*, C(3''')); 68.4 (*t*, C(6')); 65.7 (*d*, C(4''')); 63.6 (*t*, C(5'')); 63.4 (*d*, C(5')); 61.5 (*d*, C(2')); 59.1 (*d*, C(3)); 58.0 (*d*, C(1)); 56.5 (*d*, C(3'')); 50.7 (*t*, C(6''')); 31.4 (*t*, C(2)); 20.89, 20.85, 20.78, 20.73, 20.68, 20.55 (6*q*, 6 *Me*C=O). HR-MALDI-MS: 1032.3009 (100, $[M + Na]^+$, $C_{36}H_{47}N_{15}NaO_{20}^+$; calc. 1032.3014).

4',6'-O-*Methyleneparomomycin* (**21**). A soln, of **35** (100 mg, 99 μmol) in 0.1 M MeONa in MeOH (4 mL) was stirred at 26 °C for 6 h, neutralized with *Amberlite IR-120* (H^+ form), filtered, and evaporated. A soln. of the residue in THF (3 mL) was treated with 0.1 N NaOH (1.5 mL, 0.15 mmol) and 1 M PMe_3 in THF (0.69 mL, 0.69 mmol), stirred at 60 °C for 6 h, and evaporated. FC (MeOH/25% aq. NH_3 4:1) gave crude **21** (*ca*. 90% pure, 49 mg, *ca*. 72%) as a colorless powder. R_f (MeOH/25% aq. NH_3 4:1) 0.23. IR (ATR): 3211*m*, 3042*m*, 2940*m*, 1565*m*, 1403*m*, 1397*m*, 1108*s*, 970*m*. ^{1}H-NMR (600 MHz, D_2O): 5.92 (*d*, *J* = 4.2, H–C(1')); 5.38 (*d*, *J* =

2.1, H–C(1’’)); 5.25 (*d*, *J* = 1.6, H–C(1’’’)); 5.04 (*d*, *J* = 6.5, $OCH_{eq}O$); *ca*. 4.69 (*d*, *J* = 6.5, overlapping with the HDO signal, $OCH_{ax}O$); 4.48 (*dd*, *J* = 6.9, 4.7, H–C(3’’)); 4.40 (*dd*, *J* = 4.7, 2.0, H–C(2’’)); 4.29 (*ddd*, *J* = 6.7, 3.8, 1.6, H–C(5’’’)); 4.23–4.19 (*m*, H_{eq}–C(6’), H–C(4’’), H–C(3’’’)); 4.14 (*t*, *J* = 10.0, H–C(3’)); 4.00 (*dd*, *J* = 10.0, 9.2, H–C(4)); 3.95 (*t*, *J* = 9.0, H–C(5)); 3.87 (*dd*, *J* = 12.3, 2.9, H_a–C(5’’)); 3.79–3.77 (*m*, H–C(4’’’)); 3.76–3.66 (*m*, H–C(6), H–C(5’) H_b–C(5’’)); 3.60–3.55 (*m*, H–C(3), H_{ax}–C(6’), H–C(2’’’)); 3.484 (*dd*, *J* = 10.6, 3.9, H–C(2’)); 3.479 (*dd*, *J* = 10.3, 9.7, H–C(4’)); 3.38 (*dd*, *J* = 13.6, 7.0, H_a–C(6’’’)); 3.35–3.29 (*m*, H–C(1)); 3.31 (*dd*, *J* = 13.6, 3.8, H_b–C(6’’’)); 2.49 *(dt*, *J* = 12.6, 4.1, H_{eq}–C(2)); 1.88 (*q*, *J* = 12.6, H_{ax}–C(2)). ^{13}C-NMR (150 MHz, D_2O): 110.3 (*d*, C(1’’)); 95.8 (*d*, C(1’)); 95.1 (*d*, C(1’’’)); 93.5 (*t*, OCH_2O); 84.7 (*d*, C(5)); 81.3 (*d*, C(4’’)); 79.6 (*d*, C(4’)); 75.5 (*d*, C(4)); 74.9 (*d*, C(3’’)); 73.3 (*d*, C(2’’)); 72.5 (*d*, C(6)); 70.3 (*d*, C(5’’’)); 67.7 (*d*, C(3’’’)); 67.3 (*t*, C(6’)); 67.2 (*d*, C(4’’’)); 66.1 (*d*, C(3’)); 64.2 (*d*, C(5’)); 60.2 (*t*, C(5’’)); 54.3 (*d*, C(2’)); 50.8 (*d*, C(2’’’)); 49.9 (*d*, C(1)); 48.5 (*d*, C(3)); 40.4 (*t*, C(6’’’)); 28.0 (*t*, C(2)). HR-MALDI-MS: 628.3039 (69, $[M + H]^+$, $C_{24}H_{46}N_5O_{14}^+$; calc. 628.3036).

6,3’,2”,5”,3”’,4”’-Hexa-O*-acetyl-1,3,2’,2”’,6”’-pentadeamino-1,3,2’,2”’,6”’-penta-azido-4’,6’*-O*-ethylideneparomomycin* (**36).** To a soln. of 21 mg of **30** in 1 ml acetaldehyde was added 1 mg $FeCl_3$ (ca. 0.3 equiv.), and the mixture was kept for 5 min at 0 °, diluted with AcOEt, filtered over Celite, and washed with 0.1M aq. NaOH. The aq. layer was extracted twice with AcOEt. The combined org. layers were washed with brine, dried ($MgSO_4$), filtered, and evaporated. FC (hexane/AcOEt 8:2 to 6:4) gave 18 mg of **36** (84%). White solid. R_f (hexane/AcOEt 1:1) 0.48. ^{1}H-NMR (300 MHz, $CDCl_3$): 5.80 (*d, J* =4.1, H-C(1’)); 5.46 (*t, J* = 10.0, H-C(3’)); 5.33 (*d, J* = 2.5, H–C(1’’)); 5.02 (*t, J* = 2.8,H–C(3’’’)); 4.92 (*t, J* = 9.3, H–C(6)); 4.92–4.84 (*m*, H-C(2’’), H–C(1’’’)); 4.70 (br. *s*, H–C(4’’’)); 4.67 (*q*, *J* = 5.0, CH_3CH); 4.46–4.36 (*m*, H_a-C(5’’), H-C(3’’)); 4.29 ((*td, J* = 5.0, 2.2 HC(4’’)); 4.32–4.19 (*m*, H–C(5’), H_a-C(6’), H_b-C(5’’), H-C(5’’’)); 3.88 (*t, J* = 8.4, H–C(5)); 3.68–3.35 (*m*, H_b-C(6’),H-C(4), H-C(4’), H_a-C(6’’’), H-C(3), H-C(1)); 3.34–3.30 (*m*, H-C(2’’’)); 3.25 (*dd, J* = 13.1, 4.1Hb-C(6’’’)); 3.01 (*dd,*

J = 10.6, 4.1 H-C(2')); 2.38 (d*t*, *J* = 13.4, 4.4 H_{eq}-C(2)); 2.171, 2.165. 2.157, 2.143, 2.11, 2.08 (6*s*, 6 AcO); 1.61 (*q*, *J* = 12.5 H_{ax}-C(2)); 1.33 (*d*, *J* = 5.0, *Me*CH). ^{13}C-NMR (75 MHz, $CDCl_3$): 170.56, 169.96, 169.92, 169.62, 169.51, 168.36 (6*s*, 6 C=O); 107.04 (*d*, C(1'')); 99.69, 99.05 (2*d*, Me*C*H, C(1'''));); 97.53 (*d*, C(1')); 82.19 (*d*, C(5)); 79.21 (*d*, C(4'')); 78.50 (*d*, C(4')); 75.79 (*d*, C(3'')); 75.35 (*d*, C(6)); 74.76(*d*, C(2'')); 73.59(*d*, C(5''')); 69.04 (*d*, C(3')); 68.71, 68.21 (*d*, C(3'''), *t*, C(6')); 65.73 (*d*, C(4''')); 63.63 (*d*, C(5'')); 63.27 (*d*, C(5')); 61.55 (*d*, C(2')); 58.97 (*d*, C(3)); 58.06 (*d*, C(1)); 56.49 (*d*, C(2''')); 50.69 (*t*, C(6''')); 31.45 ((*t*, C(2)); 29.81 (*q*, *Me*CH); 21.00, 20.93, 20.41 (3*q*, 6 MeC=O), *d* of C(4) hidden by solvent peaks. HR-MALDI-MS: 1047.3167 (46); 1046.3153 (100, $[M + Na]^+$, $C_{37}H_{49}N_{15}NaO_{20}^+$; calc. 1046.3176).

4',6'-O-*Ethylideneparomomycin (***22**). A soln. of 29 mg of **36** in CH_2Cl_2/MeOH 1:4 was treated with NaOMe (12 equiv.), and stirred at 25°. The mixture was treated with *Amberlite IR-120 (H^+)*, filtered, and evaporated. FC ($CHCl_3$/AcOEt/MeOH 1:1:0 → 3:3:0.3) gave 20 mg of *1,3,2',2'',6''-Pentadeamino-1,3,2',2'',6''-pentaazido-4',6'*-O-*ethylideneparomomycin* (**37**) (92%). White solid. R_f ($CHCl_3$/AcOEt/MeOH 3:3.0.5) 0.24.

Under N_2, a soln. of 18 mg of **37** in THF was treated with 0.1M aq. NaOH (2 equiv.) and 1M aq. PMe_3 in THF (6 equiv.), stirred at 60°, and evaporated. FC (THF, THF/MeOH, MeOH, MeOH/25% aq. NH_3 49:1 → MeOH/25% aq. NH_3 4:1) gave 15 mg of 31 mg (99%) of **31**. White solid. R_f (MeOH/25% aq. NH_3 4:1) 0.27. IR (ATR): 3286*w*, 2888*w*, 1664*w*, 1571*w*, 1472*w*, 1392*w*, 1341*w*, 1102*s*, 1017*s*, 995*s*, 937*w*, 907*w*. ^{1}H-NMR (500 MHz, D_2O): 5.51 (d, J = 3.9, H–C(1')); 5.38 (d, J = 2.4, H–C(1'')); 5.07 (d, J = 1.8, H–C(1''')); 4.92 (q, J = 5.1; C*H*CH_3); 4.48 (dd, J = 6.7, 5.0, H–C(3'')); 4.34 (dd, J = 4.9, 2.4, HC(2'')); 4.20–4.15 (m, H–C(4''), H–C(5''')); 4.16 (dd, J = 10.6, 5.0, H_a–C(6'); 4.09 (t, J = 3.3, H–C(3''')); 3.90–3.85 (m, H–C(5'), H_a–C(5'')); 3.79 (t, J = 9.7, H–C(3')); 3.77–3.70 (m, H–C(5), H_b–C(5''), H–C(4''')); 3.69 (t, J = 10.5, H_b–C(6')); 3.54–3.48 (m, H–C(4), H–C(4')); 3.43 (t, 10.0, H–C(6)); 3.32 (dd, J = 13.5, 7.7, H_a–C(6''')); 3.25 (dd J = 13,6, H_b–C(6''')); 3.18–3.17 (m, H–C(2''')); 3.06–2.94 (m, H–C(1), H–C(3)); 2.96 (dd, J = 10.1, 3.9, H–C(2')); 2.09 (dt, J = 12.9, 4.2, H_{eq}–C(2)); 1.38–1.31 (m, H_{ax}–

C(2)); 1.36 (d J = 5.1 C*H*$_3$CH). ^{13}C–NMR (126 MHz, D_2O, data from a HSQC spectrum): 111.54 (d, C(1’’)); 102.71 (d, CH_3*C*H)); 101.63 (d, C(1’)); 100.87 (d, C(1’’’)); 86.99 (d, C(5)); 83.89 (d, C(4), C(4’’)); 82.92 (d, C(4’)); 78.32, 78.08 (2d C(6), C(3’’)); 76.05 (d, C(2’’)); 74.19 (d, C(5’’’)); 72.53 (d, C(3’), C(3’’’)); 71.01 (d, C(4’’’)); 70.20 (t, C(6’)); 66.27 (d, C(5’)); 63.36 (t, C(5’’)); 58.50 (d, C(2’)); 54.75 (d, C(2’’’)); 53.08 (d, C(3)); 52.20 (d, C(1)); 43.39 (t, C(6’’’)); 36.26 (t, C(2)); 21.90 (*q*, *C*H_3). HR-MALDI-MS: 665.3048 (31, 664.3018 (100, $[M + Na]^+$, $C_{25}H_{47}N_5NaO_{14}^+$; calc. 664.3012).

References

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2. **Pathak R, Perez-Fernandez D, Nandurdikar R, Kalapala SK, Böttger EC, Vasella A.** 2008. Synthesis and evaluation of paromomycin derivatives modified at C(4 '). Helv. Chim. Acta **91**:1533-1552.

Scheme 1

a) CH_3I or RBr, NaH, TBAI, DMF; 68% of **3**; 88% of **4**; 79% of **5**; 86% of **6**; 75% of **7**; 77% of **8**. *b*) CAN, MeCN/H_2O 9:1; 0.1 M aq. NaOH, 1 M PMe_3, THF, 60 °C; 60% of **9**; 64% of **10**; 49% of **11**; 64% of **12**; 75% of **13**; 55% of **14**; 52% of **15**. *c*) AcOH/H_2O 1:1, lyophilisation. *d*) $BH_3{\cdot}SMe_2$, THF; 0.1 M NaOH, 30% H_2O_2; 64%.

Scheme 2

a) NaH, DMF, Bu_4NI, **25**, 58%. *b)* TsOH.H_2O. MeOH, CH_2Cl_2, 72%. *c)* 1. $NaIO_4$, $NaHCO_3$, H_2O; 2. $NaBH_4$, MeOH, CH_2Cl_2, 79%. *d)* H_2, $Pd(OH)_2$, 11%. *e)* PMe_3, 0.1 M aq. NaOH, THF, 89%. *f)* H_2, $Pd(OH)_2$, MeOH/H_2O/AcOH, 19%.

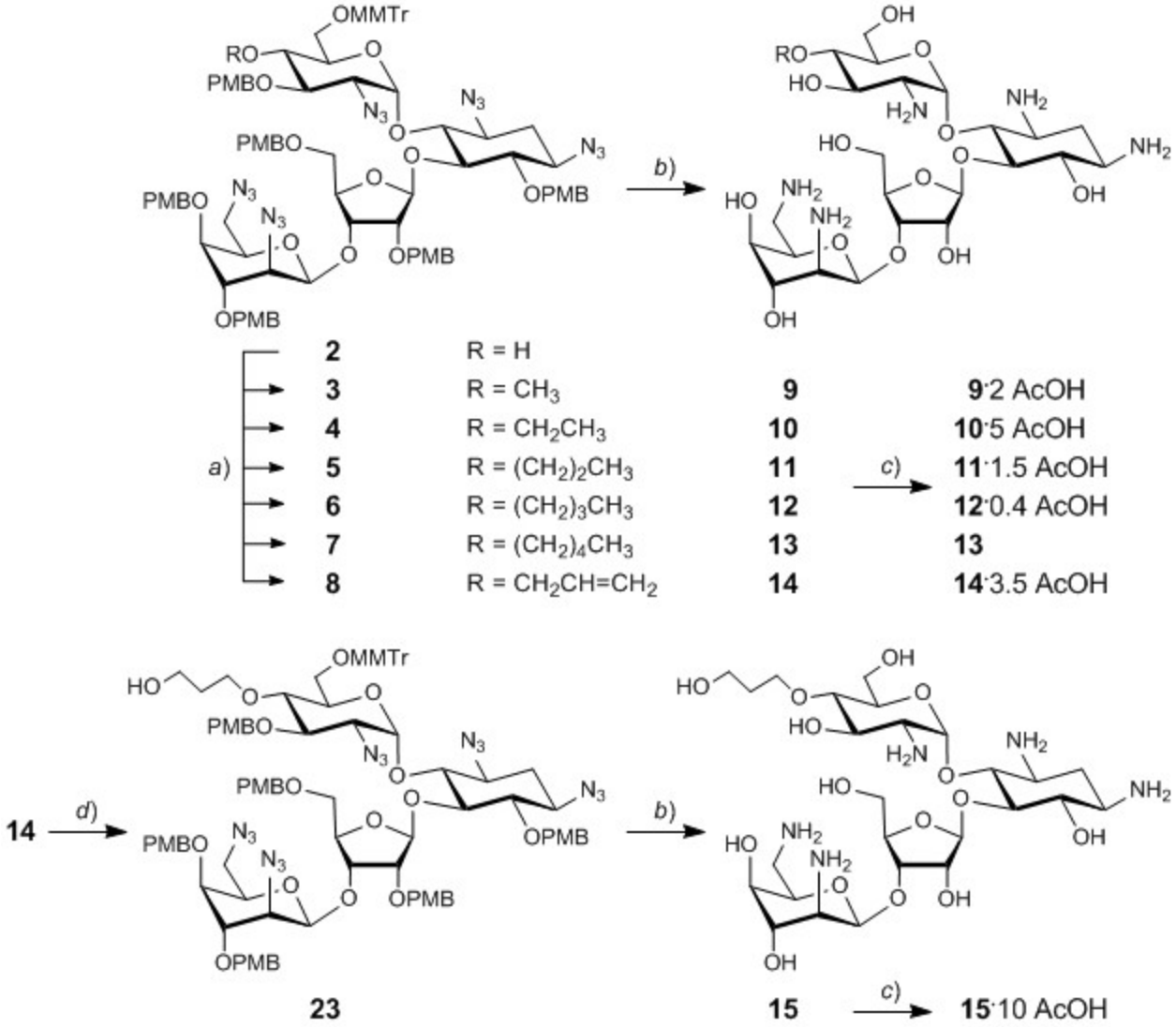
Scheme 3

a) PivCl, DMAP, pyridine; 72%. *b*) $FeCl_3$, $CH_2(OMe)_2$, 26 °C; 97%. *c*) As *b*), 0 °C; 82%. *c*) NaOMe, MeOH; 0.1 M aq. NaOH, 1 M PMe_3, THF, 60 °C; 83% of **18**; 82% of **19**. *e*) AcOH/H_2O 1:1, lyophilisation.

Scheme 4

a) $FeCl_3$, $CH_2(OMe)_2$, 26 °C; 80%. *b*) TMSCl/DMSO, CH_2Cl_2, reflux; 45%. *c*) NaOMe, MeOH; 0.1 M aq. NaOH, 1 M PMe_3, THF, 60 °C; 84% of **20**; 72% of **21**. *d*) AcOH/H_2O 1:1, lyophilisation. *e)* acetaldehyde, $FeCl_3$, 0°; 84%. *f)* NaOMe, MeOH, CH_2Cl_2, then Amberlite IR 120 (H^+); 92%. g) 0.1 M aq. NaOH, 1 M PMe_3, THF, 60 °C; 99%.

Scheme 1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PMBO
N3
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OPMB
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NH2
HO
NH2
NH2
HO
NH2
OH
OH
OH
a)
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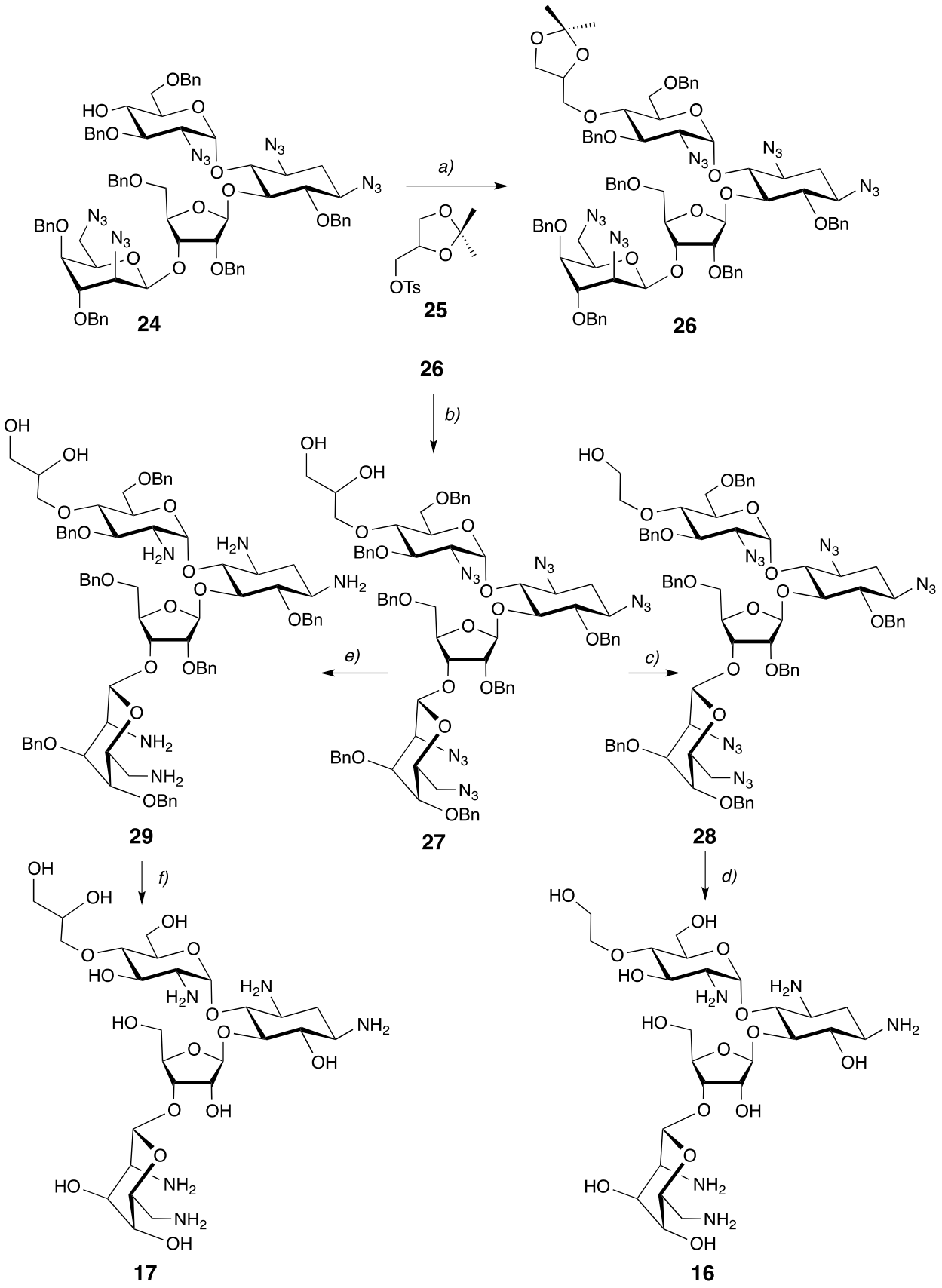
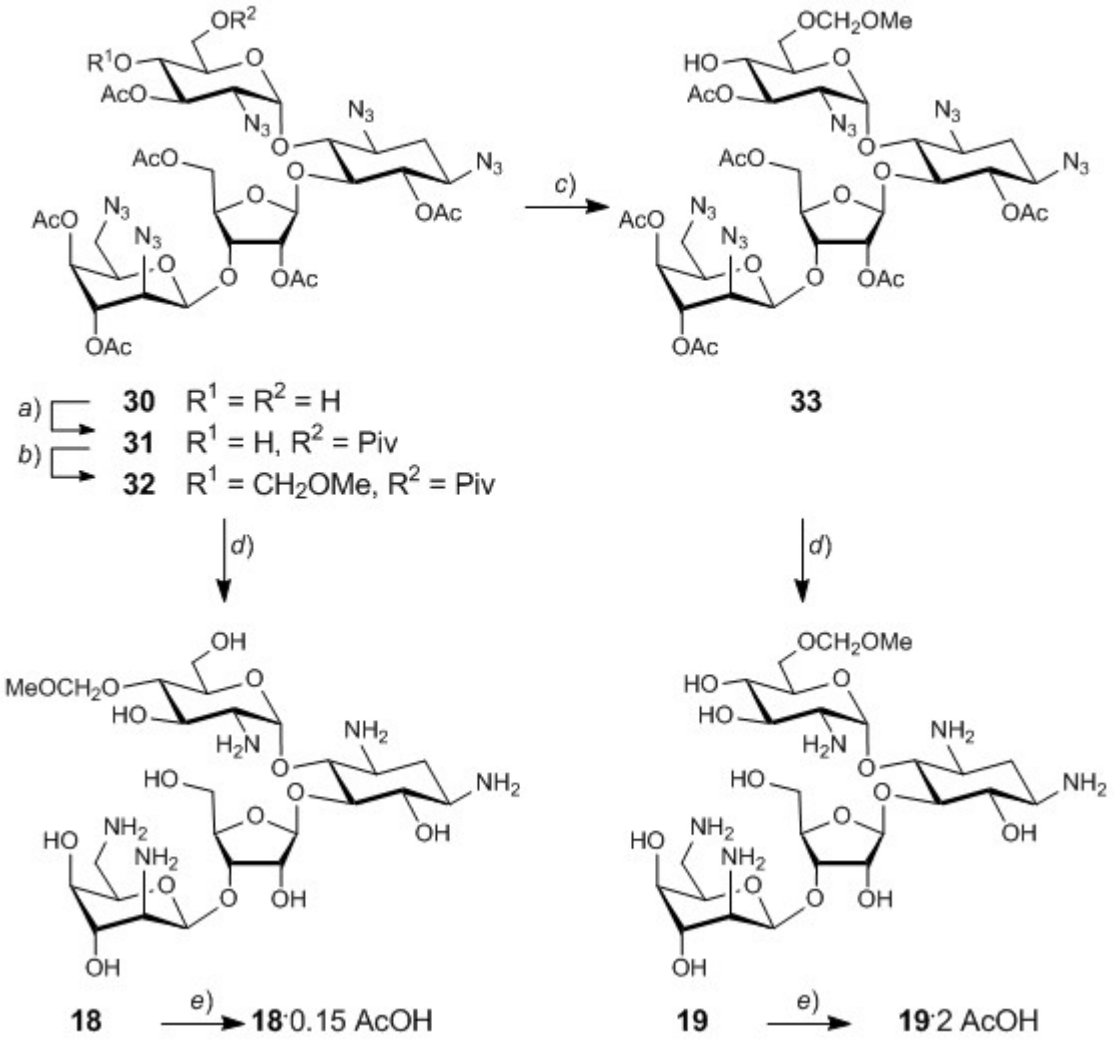
3 R = CH3
4 R = CH2CH3
5 R = (CH2)2CH3
6 R = (CH2)3CH3
7 R = (CH2)4CH3
8 R = CH2CH=CH2
9
10
11
12
13
14
c)
9·2 AcOH
10·5 AcOH
11·1.5 AcOH
12·0.4 AcOH
13
14·3.5 AcOH
14
d)
HO
23
15
15·10 AcOH

Scheme 2



Scheme 3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R1O
AcO
N3
O
OAc
c)
OCH2OMe
HO
a)
b)
30 R1 = R2 = H
31 R1 = H, R2 = Piv
32 R1 = CH2OMe, R2 = Piv
33
d)
MeOCH2O
H2N
NH2
NH
OH
18
e)
18·0.15 AcOH
19
19·2 AcOH

Scheme 4