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Total synthesis of a protected form of 2,6-anhydro-5-azido-3,5-dideoxy-2-*C*-hydroxymethyl-L-*allo*-heptose; a potential precursor of analogs of *C*-glycosides of neuraminic acid

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Abstract

The title aldehyde (–)-**3** and its enantiomer (+)-**3** have been prepared starting from furfuryl alcohol and acetone. The method involves the diastereoselective [4+3]-cycloaddition of 2-[(benzyloxy)methyl]furan and 1,3-dibromo-2-oxyallyl cation giving adduct (±)-**4** that was converted with high yield into (±)-(2*RS*,5*RS*,6*SR*)-5-azido-2-[(benzyloxy)methyl]-2,3,5,6-tetrahydro-2,6-bis(hydroxymethyl)-4*H*-pyran-4-one ((±)-**9**). Ketone (±)-**9** was then transformed with high selectivity into (±)-(2*RS*,4*RS*,5*SR*,6*RS*)-5-azido-2-[(benzyloxy)methyl]-2,3,5,6-tetrahydro-4-[(triethylsilyl)oxy]-6-{[(triisopropylsilyl)oxy]methyl}-2*H*-pyran-2-methanol (±)-**3** that was resolved by the Alexakis–Mangeney method (column chromatography of aminals derived from (1*R*,2*R*)-1,2-diphenylethylenediamine). The absolute configuration of (–)-**3** was established by circular dichroism and the Dale–Mosher method on derivatives.

1. Introduction

Sialic acid containing glycoconjugates are cell-type specific markers that play vital roles in a great number of physiologically and pathologically important processes. These include embryogenesis, organ development, immune defense, migration and selection of leukocytes, metastasis of cancer cells, as well as inflammation and the infection by pathogens.[1] For instance, the influenza infection is an example of cell/virus interaction mediated by sialic acid. Virus-releasing enzyme influenza sialidase inhibitors have been used as drugs against the common flu.[2] Inhibitors of sialidases and of sialyltransferases are quite often sialic acid analogs.[3,4] A new class of potential inhibitors are *C*-glycosides of neuraminic acid and analogs.[5] Disaccharides and

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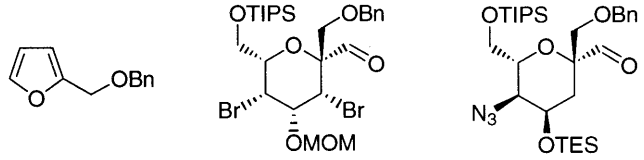
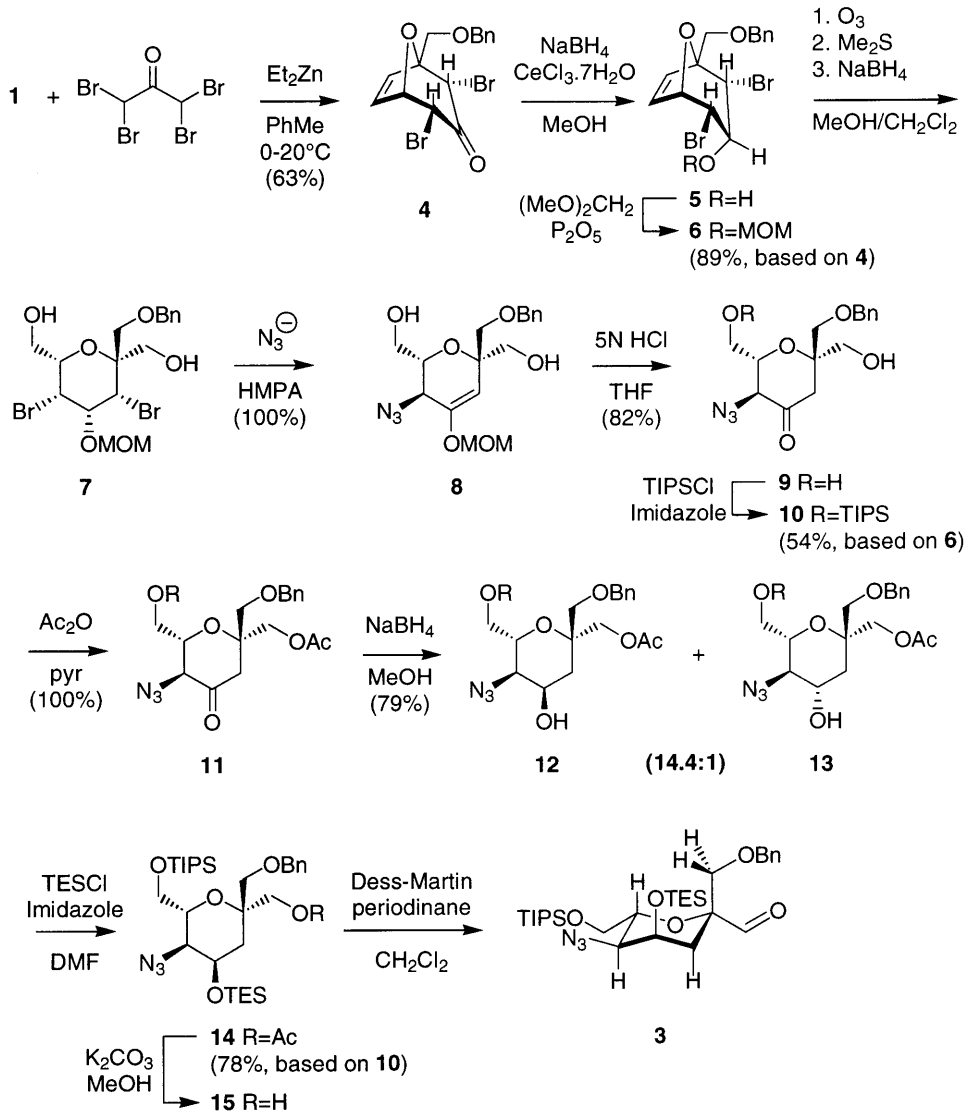
oligosaccharides[6] have limited applications as therapeutic agents because of their susceptibility to enzymatic hydrolysis by glycosidases. One strategy towards by-passing this problem is to replace the glycosidic oxygen atom with a sulfur[7] or by a carbon linker.[8] Our laboratory has proposed recently general approaches to the construction of libraries of C(1→3),[9] C(1→2) and C(1→4)-linked disaccharides[10] by condensation of sugar-derived carbaldehydes with bicyclic enolates or enol triflates. In a preliminary communication,[11] we presented the conversion of 2-[(benzyloxy)methyl]furan **1** into a protected form of racemic 3,5-dibromo-3,4,5,6-tetrahydro-4-hydroxy-2,6-bis(hydroxymethyl)-2*H*-pyran-2-carboxaldehyde **2** that could be used to carry out cross-aldolizations, opening an approach to the synthesis of *C*-disaccharide analogs mimicking sialic acid glycosides. We report here the preparation the enantiomerically enriched (>98% ee) 2,6-anhydro-5-azido-3,5-dideoxy-2-*C*-hydroxymethyl-L-*allo*-heptose derivatives (−)-**3** also starting from **1**. Orthogonal protection of the alcoholic moieties in (−)-**3** leaves open the possibility of oxidizing the 2-*C*-hydroxymethyl group into a carboxylic acid, to prolong the carbon chain at C-7 and to invert center C-4 in order to approach neuraminic acid structure.



1 **2** **3**

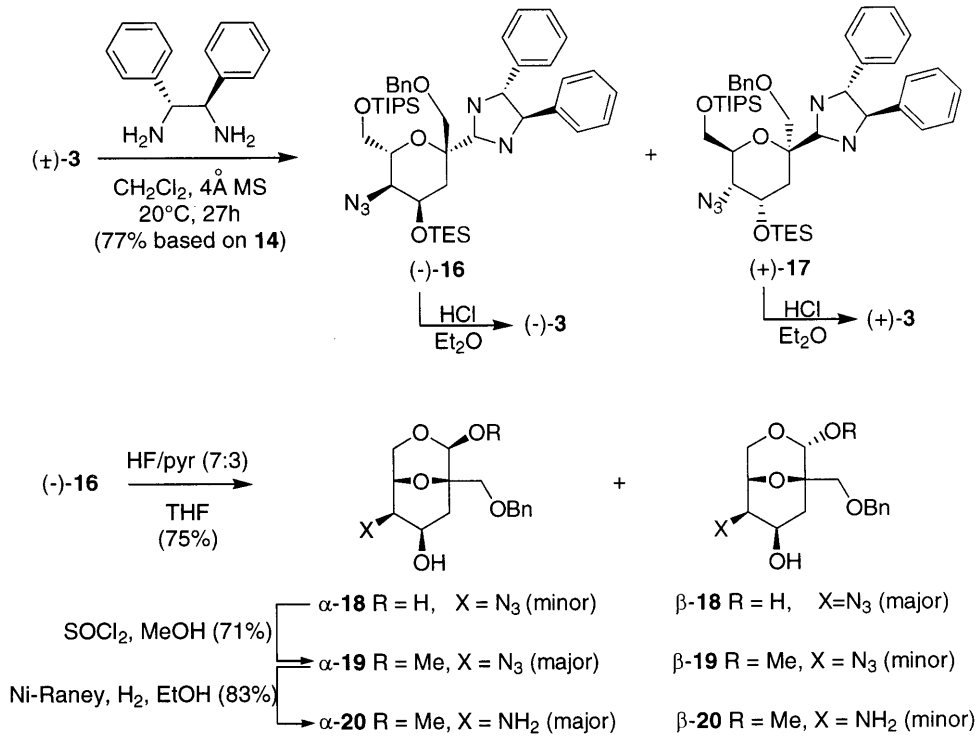
2. Results and discussion

Applying the method of Mann,[12] we found that furan **1** (obtained by benzylation[13] of furfuryl alcohol) undergoes smooth [4+3]-cycloaddition with the 1,3-dibromo-2-oxyallyl cation generated from 1,1,3,3-tetrabromopropan-2-one[14] in the presence of Et_2Zn giving adduct (±)-**4** in 63% yield, the *endo* relative configuration of the 2- and 4-bromo substituents being established by the ^{1}H NMR spectrum (^3J(H,H), 2D-NOESY). Using the Luche procedure,[15] ketone (±)-**4** was reduced into *endo*-alcohol (±)-**5** quantitatively. This alcohol was protected as its MOM ether (±)-**6** (89%, two steps). Ozonolysis of the alkene moiety of (±)-**6**, followed by reductive work-up (Me_2S, then $NaBH_4$), provided the 3,4,5,6-tetrahydro-2*H*-pyran derivative (±)-**7** nearly quantitatively. Treatment of (±)-**7** with NaN_3 (5 equiv.) or tetramethylguanidinium azide[16] displaced the less sterically hindered bromide at C-5[17] concomitantly with HBr elimination between C-3 and C-4 giving the azido-enol ether (±)-**8** quantitatively. The displacement reaction occurred with complete inversion as demonstrated with the structure of (±)-**8**. The latter was established by its spectral data, including its ^{1}H NMR spectrum ($^3J(H_{axial}\text{-}5,H_{axial}\text{-}6) = 9.1$ Hz, 2D-NOESY). Acidic hydrolysis[18] of (±)-**8** liberated ketone (±)-**9**. Selective monosilylation of the less sterically hindered primary alcohol at C-7 was accomplished using 1.1 equiv. of triisopropylsilyl chloride and imidazole.[19] This furnished (±)-**10** in 54% yield based on (±)-**6**. Acetylation of (±)-**10** gave (±)-**11** (100%). The ketone (±)-**11** was reduced with $NaBH_4$ in methanol giving a 14.4:1 mixture of alcohols (±)-**12** and (±)-**13** that was silylated with triethylsilyl chloride and imidazole.[20] This furnished pure (±)-**14** [78% based on (±)-**10**], after purification by flash chromatography on silica gel. Alkaline methanolysis[21] liberated alcohol (±)-**15** that was oxidized with the Dess–Martin periodinane[22] to (±)-**3** (Scheme 1).



Scheme 1. Synthesis of racemic (±)-**3**

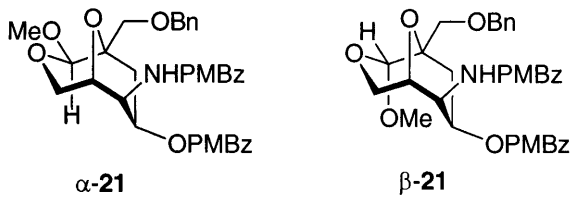
Resolution of aldehyde (±)-**3** was achieved applying the method of Alexakis and Mangeney[23] using (1*R*,2*R*)-(+)-1,2-diphenylethylenediamine that gave a 1:1 mixture of aminals (−)-**16** and (+)-**17** in 77% yield based on (±)-**14**. They were separated by column chromatography on silica gel. Acidic extraction of (−)-**16** (1N HCl/Et_2O) liberated (−)-**3** in 95% yield and the chiral diamine that was recovered in 91% yield. The ^1H NMR spectrum of (−)-**3** is consistent with the chair conformation shown in Scheme 1 ($^3J(H_{axial}\text{-}5,H_{axial}\text{-}6) = 9.2$ Hz, 2D-NOESY). Desilylation of (−)-**16** with HF in pyridine[24] led to simultaneous aminal hydrolysis and hemiacetal formation giving a 2:1 mixture of β-**18** and α-**18**. It was converted into a 1.7:1 mixture of the corresponding methyl glycosides α-**19** and β-**19** on treatment with methanol and $SOCl_2$. Reduction of the azides of **19** by hydrogenation catalyzed with Raney-nickel afforded a 1.7:1 mixture of α-**20** and β-**20** (Scheme 2).



Scheme 2. Resolution of (±)-**3**

Treatment of this mixture with 3 equivalents of *p*-methoxybenzoyl chloride in pyridine with a catalytical amount of 4-dimethylaminopyridine gave the corresponding amido-esters α-**21** and β-**21** that were separated by high pressure liquid chromatography. The circular dichroism spectra (Fig. 1) of these compounds showed positive Cotton effects at $\lambda = 260$ nm and weak Cotton effects at $\lambda = 240$ nm for a maximum of absorption in the UV spectrum appearing at $\lambda = 248$ nm ($\varepsilon = 15800$). This is indicative of the existence of an exciton due to the coupling of the *p*-methoxybenzoate at C-7 and the *p*-methoxybenzamido at C-6. The positive Cotton effect at the highest wavelength is consistent with a positive coupling between these two chromophores,[25] as expected for both α-**21** and β-**21**. The tetrahydropyran moieties of these compounds adopt preferred chair conformation as shown in Fig. 1. This was confirmed by the ^3J(H,H) coupling constants measured in their ^{1}H NMR spectra, thus establishing the absolute configuration of these compounds and of their precursors. This allowed us to assign the L-*allo*-heptose configuration to (−)-**3**. Because of the distance separating the benzyloxy group from the *p*-methoxybenzoate and *p*-methoxybenzamide chromophores in α-**21** and β-**21**, the benzyloxy group is not expected to contribute significantly to the sign of the highest wavelength Cotton effect ($\lambda = 260$ nm) arising from the exciton coupling of the two *p*-methoxybenzoyl chromophores. It may nevertheless contribute to the lower wavelength Cotton effect ($\lambda = 240$ nm) making the latter effect less negative than expected for an ideal *p*-methoxybenzoate and *p*-methoxybenzamido couplet.

The enantiomeric excess (ee) of (−)-**3** was determined by Mosher's esters **22** derived from the mixture of alcohols α-**19** and β-**19** and from (*S*)-(+)- and (*R*)-(−)-(trifluoromethyl)(methoxy)phenylacetyl chloride. By ^{19}F NMR and comparing with the satellite



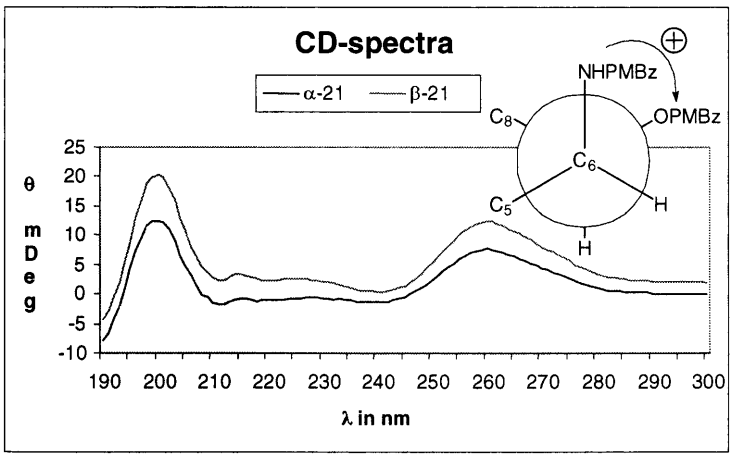
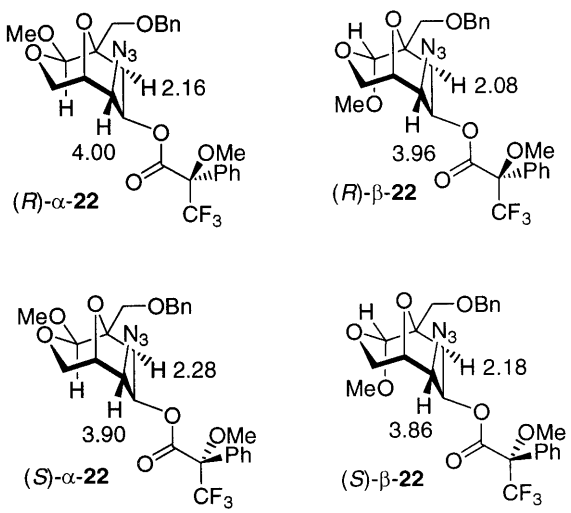


Figure 1. Circular dichroism of α-**21** and β-**21**

signals due to the ^{13}C–^{19}F couplings, the diastereomeric excesses of esters (*R*)-α-**22**, (*R*)-β-**22**, (*S*)-α-**22** and (*S*)-β-**22** were better than 98%. Applying the proton chemical shift criteria of Dale and Mosher[26] (see Scheme 3, δ_H of H_{eq}-2, H-4), the absolute configuration shown for these compounds is confirmed.



Scheme 3. Mosher's esters; the Dale–Mosher method for the determination of the absolute configuration (δ_H ($CDCl_3$, 25°C) ppm)

3. Conclusions

Starting from inexpensive starting materials such as furfuryl alcohol and acetone, (−)-**3**, a protected form of 2,6-anhydro-5-azido-3,5-dideoxy-2-*C*-hydroxymethyl-L-*allo*-heptose, has been prepared in 14% overall yield and with high enantiomeric excess (>98%). This compound is a potential precursor of *C*-glycosides including neuraminic acid derivatives. The method relies on the diastereoselective [4+3]-cycloaddition of 1,3-dibromo-2-oxyallyl cation to 2-[(benzyloxy)methyl]furan and on resolution via aminals derived from (1*R*,2*R*)-(+)-1,2-diphenylethylenediamine. Although it involves 16 steps, the isolation and purification of only seven intermediates is required. At the same time, the enantiomeric form with the D-*allo* configuration is obtained with the same ease. Aldehydes (−)-**3** and (+)-**3** will be used to generate *C*-linked disaccharides and analogs of biological interest, applying methodology already available.[9–11]

4. Experimental section

General, see Ref. 27. Circular dichroism spectra were recorded on a Jobin Yvon Mark VI instrument using cubic quartz cell (length 0.1 cm) and calibrated with D-(+)-10-camphorsulfonic acid.

*4.1. (1*RS,*2*RS,*4*SR,*5*RS*)-1-[(Benzyloxy)methyl]-2*-endo,*4*-endo-*dibromo-8-oxabicyclo[3.2.1]-oct-6-en-3-one (±)-**4***

A 1.1 M soln of Et_2Zn in toluene (50 mL, 55 mmol) was added dropwise to a soln of 1,1,3,3-tetrabromopropan-2-one[14] (15 g, 40.1 mmol) and 2-[(benzyloxy)methyl]furan **1**[13] (5 g, 26.6 mmol) in toluene (250 mL) stirred at 0°C. After stirring at 0°C for 105 min, the mixture was allowed to warm to 20°C and stirred for a further 75 min. After the addition of EtOAc (50 mL) and of a sat. aq. soln of NH_4Cl (50 mL), the mixture was filtered through a pad of Celite (6 cm). The aq. phase was extracted with EtOAc (50 mL, three times). The combined org. extracts were washed with a sat. soln of NH_4Cl (20 mL, three times), dried ($MgSO_4$) and concentrated. The residue resulting from 12 reaction runs were combined and recrystallized from light petroleum ether/Et_2O (3:1): white crystals (28.3 g). FC of the residual red oil (silica gel, light petroleum ether/Et_2O (3:1), R_f (**4**) = 0.25) afforded more white solid **4** (32.6 g) and an orange oil (20.7 g). Yield of (±)-**4**: as crystals (60.9 g, 47.5%); as oil (20.7 g, 16%). Mp: 72–73°C. UV (CH_3CN): λ_{max} = 210 nm (ε = 8300 [dm^3 cm^{-1} mol^{-1}]). IR (KBr): 3060, 2950, 2870, 2360, 1745, 1495, 1455, 1370, 1335, 1310, 1265, 1215, 1075, 1010, 940, 865, 850, 820 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): 7.38–7.17 (m, 5H(Ph)); 6.55 (dd, ^3J(H-6,H-7) = 6.1 Hz, ^3J(H-6,H-5) = 1.8 Hz, H-6); 6.28 (d, ^3J(H-7,H-6) = 6.1 Hz, H-7); 5.2 (dd, ^3J(H-5,H-4) = 4.8 Hz, ^3J(H-5,H-6) = 1.8 Hz, H-5); 5.16 (s, H-2); 4.87 (d, ^3J(H-4,H-5) = 4.8 Hz, H-4); 4.72, 4.64 (2d, ^2J = 12.1 Hz, CH_2(Bn)); 4.08, 3.80 (2d, ^2J = 10.9 Hz, 2H-1′). ^{13}C NMR ($CDCl_3$, 100.6 MHz): 190.6 (s, C3); 142.7 (s, Car); 134.7 (d, ^1J = 178 Hz, C6); 133.9 (d, ^1J = 173 Hz, C7); 128.5 (d, ^1J = 158 Hz, 2CHar); 128.0 (d, ^1J = 161 Hz, 2CHar); 127.9 (d, ^1J = 161 Hz, CHar); 91.3 (s, C1); 82.6 (d, ^1J = 166 Hz, C5); 73.9 (t, ^1J = 142 Hz, CH_2(Bn)); 69.3 (t, ^1J = 143 Hz, C1′); 57.4 (d, ^1J = 154 Hz, C2); 54.7 (d, ^1J = 153 Hz, C4). CI-MS(NH_3): *m*/*z* 420 (3, $[M+NH_4]^+$), 402 (1, $[M^\circ]^+$), 323 (6, $[M-^{79}Br]^+$), 321 (5, $[M-^{81}Br]^+$), 277 (4), 275 (4), 217 (2), 215 (2), 121 (5), 91 (100). Anal. calcd for $C_{15}H_{14}Br_2O_3$ (402.09): C, 44.80; H, 3.50; Br, 39.70. Found: C, 44.72; H, 3.63; Br, 39.65.

4.2. (1RS,2SR,3SR,4RS,5RS)-1-[(Benzyloxy)methyl]-2-endo,4-endo-dibromo-8-oxabicyclo-[3.2.1]oct-6-en-3-endo-ol (±)-5

$NaBH_4$ (1.91 g, 50.4 mmol; 2.07 g, 54.8 mmol) were added portionwise to a soln of pure (±)-**4** (13.5 g, 33.6 mmol; 14.7 g, 36.5 mmol) and $CeCl_3 \cdot 7H_2O$ (13.8 g, 36.9 mmol; 15.0 g, 40.2 mmol) in MeOH (420 mL, 450 mL) stirred at 0°C. After 30 min, the soln resulting from two reaction runs were combined and treated with H_2O (100 mL) and 1N HCl (200 mL). The methanol was evaporated and the aq. phase was extracted with EtOAc (300 mL, four times). The combined org. extracts were washed with a sat. aq. soln of $NaHCO_3$ (100 mL, two times), dried ($MgSO_4$) and concentrated: white solid (27.8 g, 98%). An analytical sample of (±)-**5** can be obtained by FC on silica gel (EtOAc/light petroleum ether (1:3), R_f ((±)-**5**) = 0.32). Mp: 90–92°C. UV (CH_3CN): $\lambda_{max} = 213$ nm ($\varepsilon = 5700$ [$dm^3\ cm^{-1}\ mol^{-1}$]). IR (KBr): 3475, 1595, 1495, 1450, 1420, 1365, 1350, 1325, 1300, 1250, 1205, 1195, 1105, 1095, 1070, 1050, 995 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): 7.43–7.28 (m, 5H(Ph)); 6.55 (dd, ^3J(H-6,H-7) = 6.1 Hz, ^3J(H-6,H-5) = 1.8 Hz, H-6); 6.23 (d, ^3J(H-7,H-6) = 6.1 Hz, H-7); 4.88 (dd, ^3J(H-5,H-4) = 3.6 Hz, ^3J(H-5,H-6) = 1.8 Hz, H-5); 4.72 (d, ^3J(H-2,H-3) = 4.8 Hz, H-2); 4.67, 4.60 (2d, CH_2(Bn), $^2J = 12.1$ Hz); 4.48 (dd, ^3J(H-4,H-3) = 4.8 Hz, ^3J(H-4,H-5) = 3.6 Hz, H-4); 4.48 (ddd, ^3J(H-3,OH) = 5.5 Hz, ^3J(H-3,H-4) = 4.8 Hz, ^3J(H-3,H-2) = 4.8 Hz, H-3); 3.97, 3.64 (2d, $^2J = 10.9$ Hz, CH_2-C1); 2.59 (d, ^3J(OH,H-3) = 5.5 Hz, OH). ^{13}C NMR ($CDCl_3$, 100.6 MHz): 137.4 (s, Car); 135.1 (d, $^1J = 176$ Hz, C6); 135.1 (d, $^1J = 175$ Hz, C7); 128.2 (d, $^1J = 161$ Hz, 2CHar); 127.7 (d, $^1J = 159$ Hz, 2CHar); 127.7 (d, $^1J = 160$ Hz, CHar); 88.8 (s, C1); 82.7 (d, $^1J = 162$ Hz, C5); 73.9 (t, $^1J = 142$ Hz, CH_2(Bn)); 70.2 (t, $^1J = 143$ Hz, CH_2-C1); 69.1 (d, $^1J = 155$ Hz, C3); 52.3 (d, $^1J = 157$ Hz, C2); 50.4 (d, $^1J = 154$ Hz, C4). CI-MS(NH_3): m/z 422 (37, $[M+NH_4]^+$), 298 (27, $[M+H-OCH_2Ph]^+$), 244 (6), 227 (8), 201 (4), 130 (78), 114 (40), 108 (22), 91 (100). Anal. calcd for $C_{15}H_{16}Br_2O_3$ (404.10): C, 44.70; H, 3.75; Br, 39.60. Found: C, 44.63; H, 3.85; Br, 39.55.

4.3. (1RS,2SR,3SR,4SR,5RS)-1-[(Benzyloxy)methyl)-2-endo,4-endo-dibromo-3-(methoxy-methoxy)-8-oxabicyclo[3.2.1]oct-6-ene (±)-6

P_2O_5 was added portionwise until completion of reaction to a soln of crude (±)-**5** (13.8 g, 34.2 mmol) in a mixture of CH_2Cl_2 (135 mL) and dimethoxymethane (100 mL) stirred at 20°C. The mixtures resulting from two runs were combined and treated with CH_2Cl_2 (200 mL) and a sat. aq. soln of NH_4Cl (until destruction of residual P_2O_5). The aq. phase was extracted with CH_2Cl_2 (300 mL, four times). The combined org. extracts were washed with a sat. aq. soln of $NaHCO_3$ (100 mL, two times), dried ($MgSO_4$) and concentrated to afford a yellow solid. Recrystallization from light petroleum ether gave pure (±)-**6** as white solid (26.3 g) and FC of the residual yellow oil (silica gel, light petroleum ether/Et_2O (3:1), R_f ((±)-**6**) = 0.19) afforded 1.8 g of white (±)-**6**. (Total mass = 28.1 g; 89% based on (±)-**5**.) Mp: 59–60°C. UV (CH_3CN): $\lambda_{max} = 208$ nm ($\varepsilon = 6800$ [$dm^3\ cm^{-1}\ mol^{-1}$]). IR (KBr): 3435, 3030, 2900, 1600, 1495, 1450, 1370, 1345, 1325, 1270, 1210, 1160, 1110, 1035, 1010, 925, 895, 865, 840, 730, 700, 645 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): 7.40–7.28 (m, 5H(Ph)); 6.50 (dd, ^3J(H-6,H-7) = 6.1 Hz, ^3J(H-6,H-5) = 1.8 Hz, H-6); 6.23 (d, ^3J(H-7,H-6) = 6.1 Hz, H-7); 4.84 (dd, ^3J(H-5,H-4) = 3.3 Hz, ^3J(H-5,H-6) = 1.8 Hz, H-5); 4.75 (d, ^3J(H-2,H-3) = 4.8 Hz, H-2); 4.74 (s, CH_2(MOM)); 4.67, 4.60 (2d, $^2J = 12.4$ Hz, CH_2(Bn)); 4.52 (dd, ^3J(H-4,H-3) = 4.8 Hz, ^3J(H-4,H-5) = 3.3 Hz, H-4); 4.04 (dd, ^3J(H-3,H-4) = 4.8 Hz, ^3J(H-3,H-2) = 4.8 Hz, H-3); 3.98, 3.64 (2d, $^2J = 10.6$ Hz, CH_2-C1); 3.50 (s, Me(MOM)). ^{13}C NMR ($CDCl_3$, 100.6 MHz): 137.6 (s, Car); 134.7 (d, $^1J = 176$ Hz, C6); 133.6 (d, $^1J = 175$ Hz, C7); 128.3

(d, 2CHar); 127.9 (d, $^1J=158$ Hz, 2CHar); 127.7 (d, $^1J=159$ Hz, CHar); 99.9 (t, $^1J=164$ Hz, CH_2(MOM)); 88.9 (s, C1); 83.0 (d, $^1J=161$ Hz, C5); 76.4 (d, $^1J=148$ Hz, C3); 73.8 (t, $^1J=143$ Hz, CH_2(Bn)); 70.5 (t, $^1J=142$ Hz, CH_2-C1); 57.4 (q, $^1J=142$ Hz, Me(MOM)); 51.9 (d, $^1J=152$ Hz, C2); 50.2 (d, $^1J=153$ Hz, C4). CI-MS(NH_3): m/z 466 (35, $[M+NH_4]^+$), 342 (12, $[M+H-OBn]^+$), 306 (2, $[M-^{81}Br-OMOM]^+$), 244 (9), 227 (13), 201 (4), 91 (100). Anal. calcd for $C_{17}H_{20}Br_2O_4$ (448.15): C, 45.56; H, 4.50; Br, 35.66. Found: C, 45.63; H, 4.51; Br, 35.64.

*4.4. (2*RS,*3*SR,*4*SR,*5*SR,*6*RS*)-2-[(Benzyloxy)methyl]-3,5-dibromo-3,4,5,6-tetrahydro-4-(methoxymethoxy)-2*H*-pyran-2,6-dimethanol (±)-**7***

O_3 (3% O_3 in O_2) was bubbled through a soln of pure (±)-**6** (28.1 g, 62.6 mmol) in CH_2Cl_2/MeOH (500 mL/125 mL) containing some $NaHCO_3$ cooled at −78°C, until the soln turned blue (60 min). Then, O_2 was bubbled to eliminate the excess of ozone and Me_2S was added (10.6 mL, 144 mmol). After stirring for 15 min at −78°C, $NaBH_4$ (5.45 g, 144 mmol) was added portionwise and the soln was allowed to warm to 20°C. After 2 h at 20°C, the soln was treated with H_2O (50 mL), 1N HCl (100 mL) and the methanol was evaporated. The aq. phase was extracted with EtOAc (300 mL, four times). The combined org. layers were washed with a sat. aq. soln of $NaHCO_3$ (100 mL), dried ($MgSO_4$) and concentrated to furnish a white foam (31.5 g, 100%). An analytical sample of (±)-**7** can be obtained by FC on silica gel (EtOAc/light petroleum ether (2:1), R_f ((±)-**7**) = 0.28). UV (CH_3CN): $\lambda_{max}=268$ nm ($\varepsilon=2200$ [dm^3 cm^{-1} mol^{-1}]), 205 (7500), 196 (8500). IR (film): 3380, 2935, 1710, 1455, 1365, 1310, 1265, 1215, 1150, 1115, 1040, 965, 920, 820, 735, 700 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): 7.40–7.30 (m, 5H(Ph)); 4.82 (s, CH_2(MOM)); 4.57 (s, CH_2(Bn)); 4.48 (d, ^3J(H-3,H-4) = 4.1 Hz, H-3); 4.40 (dd, ^3J(H-4,H-5) = 4.1 Hz, ^3J(H-4,H-3) = 4.1 Hz, H-4); 4.38 (dd, ^3J(H-5,H-4) = 4.1 Hz, ^3J(H-5,H-6) = 2.8 Hz, H-5); 4.16 (ddd, $^3J=8.1$ Hz, $^3J=4.3$ Hz, ^3J(H-6,H-5) = 2.8 Hz, H-6); 4.01 (dd, $^2J=11.8$ Hz, $^3J=8.1$ Hz, H-C-C6); 3.92, 3.86 (2d, $^2J=12.0$ Hz, $BnOCH_2$-C2); 3.84 (s, $HOCH_2$-C2); 3.74 (dd, $^2J=11.8$ Hz, $^3J=4.3$ Hz, H′-C-C6); 3.47 (s, Me(MOM); 2.05 (br.s, 2H(OH)). ^{13}C NMR ($CDCl_3$, 100.6 MHz): 137.1 (s, Car); 128.6 (d, $^1J=160$ Hz, 2CHar); 128.1 (d, $^1J=161$ Hz, 2CHar); 127.8 (d, $^1J=158$ Hz, CHar); 95.8 (t, $^1J=167$ Hz, CH_2(MOM)); 78.6 (s, C2); 73.9 (d, $^1J=143$ Hz, C6); 73.8 (t, $^1J=140$ Hz, CH_2(Bn)); 72.5 (t, $^1J=144$ Hz, CH_2-C2); 71.2 (d, $^1J=143$ Hz, C4); 67.5 (t, $^1J=147$ Hz, CH_2-C2); 64.9 (t, $^1J=157$ Hz, CH_2-C6); 56.7 (q, $^1J=143$ Hz, Me(MOM)); 51.1 (d, $^1J=154$ Hz, C3); 43.3 (d, $^1J=153$ Hz, C5). CI-MS(NH_3): m/z 502 (1, $[M+NH_4]^+$), 485 (4, $[M+H]^+$), 484 (4, $[M]^+$), 469 (1, $[M-Me]^+$), 453 (10, $[M-OMe]^+$), 441 (4), 375 (2), 331 (3), 221 (2), 219 (2), 91 (100). Anal. calcd for $C_{17}H_{24}Br_2O_6$ (484.19): C, 42.17; H, 4.99; Br, 33.00. Found: C, 42.30; H, 4.90; Br, 32.95.

*4.5. (2*RS,*5*RS,*6*RS*)-5-Azido-2-[(benzyloxy)methyl]-5,6-dihydro-4-(methoxymethoxy)-2*H*-pyran-dimethanol (±)-**8***

Sodium azide (21.1 g, 325 mmol) was added to a soln of crude (±)-**7** (31.5 g, 65.1 mmol) in HMPA (350 mL) at 20°C. After stirring for 100 h at 20°C, HMPA was evaporated under reduced pressure ($P=10^{-1}$ torr, $T_{vap}=72$°C) to afford a dark oil. An analytical sample of (±)-**8** can be obtained by FC on silica gel (EtOAc/light petroleum ether (1:3), R_f ((±)-**8**) = 0.46): white foam (100%). UV (CH_3CN): $\lambda_{max}=216$ nm ($\varepsilon=4700$ [dm^3 cm^{-1} mol^{-1}]). IR (film): 3385, 2940, 2865, 2110, 1710, 1670, 1455, 1365, 1265, 1220, 1155, 1000, 925, 880, 835, 735, 700 cm^{-1}. ^1H

NMR ($CDCl_3$, 400 MHz): 7.38–7.29 (m, 5H(Ph)); 5.07, 5.01 (2d, $^2J=6.4$ Hz, CH_2(MOM)); 5.00 (d, ^4J(H-3,H-5)=0.9 Hz, H-3); 4.57, 4.52 (2d, $^2J=12.1$ Hz, CH_2(Bn)); 4.08 (dd, ^3J(H-5,H-6)=9.1 Hz, ^4J(H-5,H-3)=0.9 Hz, H-5); 3.84 (dd, $^2J=12.1$ Hz, $^3J=2.4$ Hz, H-C-C6); 3.72 (dd, $^2J=12.1$ Hz, $^3J=4.2$ Hz, H′-C-C6); 3.71, 3.53 (2d, $^2J=11.2$ Hz, BnOCH_2-C2); 3.62, 3.46 (2d, $^2J=10.6$ Hz, HOCH_2-C2); 3.59 (ddd, ^3J(H-6,H-5)=9.1 Hz, $^3J=4.2$ Hz, $^3J=4.2$ Hz, H-6); 3.47 (s, Me(MOM)). ^{13}C NMR ($CDCl_3$, 100.6 MHz): 151.1 (s, C4); 137.6 (s, Car); 128.4 (d, $^1J=160$ Hz, 2CHar); 127.8 (d, $^1J=161$ Hz, CHar); 127.5 (d, $^1J=158$ Hz, 2CHar); 100.2 (d, $^1J=159$ Hz, C3); 93.8 (t, $^1J=166$ Hz, CH_2(MOM)); 77.4 (s, C2); 73.4 (t, $^1J=143$ Hz, CH_2(Bn)); 73.2 (d, $^1J=145$ Hz, C6); 70.9 (t, $^1J=141$ Hz, CH_2-C2); 67.2 (t, $^1J=145$ Hz, CH_2-C2); 61.9 (t, $^1J=144$, CH_2-C6); 56.3 (q, $^1J=143$ Hz, Me(MOM)); 54.4 (d, $^1J=146$ Hz, C5). CI-MS(NH_3): m/z 383 (3, $[M+NH_4]^+$), 334 (1, $[M-OMe]^+$), 304 (2, $[M-OMOM]^+$), 244 (1), 192 (2), 174 (7), 148 (61), 131 (75), 103 (71), 91 (30). Anal. calcd for $C_{17}H_{23}N_3O_6$ (365.39): C, 55.88; H, 6.34; N, 11.50. Found: C, 55.72; H, 6.5; N, 11.46.

*4.6. (2*RS,*5*RS,*6*SR*)-5-Azido-2-[(benzyloxy)methyl]-2,3,5,6-tetrahydro-2,6-bis(hydroxymethyl)-4*H*-pyran-4-one (±)-**9***

5N HCl (65 mL, 325 mmol) was added to a soln of crude (±)-**8** (65 mmol) in THF (400 mL) stirred at 20°C. After 1 day, the mixture was diluted with Et_2O (400 mL). The aq. phase was extracted with Et_2O (400 mL, three times). The combined org. extracts were washed with a sat. aq. soln of $NaHCO_3$ (100 mL, two times), dried ($MgSO_4$) and concentrated. The residual dark oil was filtered through a pad of silica gel (height: 7 cm, diam. 10 cm) using CH_2Cl_2/MeOH (100:4) as eluant to afford a brown foam (20.5 g). An analytical sample of (±)-**9** can be obtained by FC on silica gel (CH_2Cl_2/MeOH (100:3), $R_f=0.08$) to afford a white foam (73–82%). UV (CH_3CN): $\lambda_{max}=211$ nm ($\varepsilon=5300$ [dm^3 cm^{-1} mol^{-1}]). IR (film): 3420, 2115, 1635, 1495, 1455, 1410, 1365, 1270, 1210, 1040, 690 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): 7.39–7.25 (m, 5H(Ph)); 4.50, 4.46 (2d, $^2J=12.1$ Hz, CH_2(Bn)); 4.05 (ddd, ^3J(H-6,H-5)=10.0 Hz, $^3J=3.3$ Hz, $^3J=2.1$ Hz, H-6); 3.99 (d, ^3J(H-5,H-6)=10.0 Hz, H-5); 3.89 (dd, $^2J=12.1$ Hz, $^3J=2.1$ Hz, H-C-C6); 3.75 (dd, $^2J=12.1$ Hz, $^3J=3.3$ Hz, H′-C-C6); 3.64, 3.42 (2d, $^2J=11.8$ Hz, BnOCH_2-C2); 3.64, 3.43 (2d, $^2J=10.3$ Hz, HOCH_2-C2); 2.77, 2.52 (2d, $^2J=14.5$ Hz, 2H-3); 2.70 (br.s, 2H(OH)). ^{13}C NMR($CDCl_3$, 100.6 MHz): 201.9 (s, C4); 136.8 (s, Car); 128.5 (d, $^1J=161$ Hz, 2CHar); 128.0 (d, $^1J=161$ Hz, CHar); 128.0 (d, $^1J=158$ Hz, 2CHar); 80.1 (s, C2); 76.0 (d, $^1J=143$ Hz, C6); 73.7 (t, $^1J=143$ Hz, CH_2(Bn)); 72.8 (t, $^1J=143$ Hz, CH_2-C2); 66.5 (t, $^1J=145$ Hz, CH_2-C2); 62.7 (d, $^1J=144$ Hz, C5); 62.5 (t, $^1J=145$ Hz, CH_2-C6); 42.9 (t, $^1J=131$ Hz, C3). CI-MS (NH_3): m/z 339 (0.3, $[M+NH_4]^+$), 294 (0.5, $[M+H-N_2]^+$), 279 (0.4), 262 (0.5), 216 (0.4), 91 (100). Anal. calcd for $C_{17}H_{23}N_3O_6$ (321.34): C, 56.07; H, 5.96. Found: C, 56.02; H, 6.05.

*4.7. (2*RS,*5*RS,*6*SR*)–5-Azido-2-[(benzyloxy)methyl]-2,3,5,6-tetrahydro-2-(hydroxymethyl)-6-{[(triisopropylsilyl)oxy]methyl}-4*H*-pyran-4-one (±)-**10***

Triisopropylsilyl chloride (13.6 mL, 64 mmol) was added dropwise (using an automatic syringe) to a soln of crude (±)-**9** (20.5 g) and imidazole (8.67 g, 127 mmol) in DMF (350 mL) stirred at −60°C. At the end of the addition (4 h), the reaction was allowed to warm to 20°C. After stirring for 21 h at 20°C, the mixture was treated with Et_2O (200 mL), and a sat. aq. soln of $NaHCO_3$ (100 mL). The aq. phase was extracted with Et_2O (200 mL, five times). The

combined org. layers were washed with a sat. aq. soln of $NaHCO_3$ (100 mL, two times), dried ($MgSO_4$), and concentrated. The residual DMF was evaporated under reduced pressure. FC (silica gel, light petroleum ether/EtOAc (3:1)) affords (±)-**10** as a colorless oil (16.2 g, 54% based on (±)-**6**, R_f ((±)-**10**) = 0.20) and (±)-**9** (2.85 g, 14% based on (±)-**6**). Converted yield of (±)-**10** (63%). UV (CH_3CN): λ_{max} = 263 nm (ε = 1000 [dm^3 cm^{-1} mol^{-1}]), 213 nm (8900). IR (film): 3440, 2945, 2885, 2115, 1730, 1650, 1455, 1270, 1095, 880, 740, 680 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): 7.40–7.24 (m, 5H(Ph)); 4.47 (br.s, CH_2(Bn)); 4.15 (d, ^3J(H-5,H-6) = 9.8 Hz, H-5); 4.07 (ddd, ^3J(H-6,H-5) = 9.8 Hz, ^3J = 2.9 Hz, ^3J = 1.7 Hz, H-6); 3.97 (dd, ^2J = 11.2 Hz, ^3J = 1.7 Hz, H-C-C6); 3.92 (dd, ^2J = 11.2 Hz, ^3J = 2.9 Hz, H′-C-C6); 3.58, 3.39 (2d, ^2J = 11.5 Hz, $BnOCH_2$-C2); 3.58, 3.41 (2d, ^2J = 10.4 Hz, $HOCH_2$-C2); 2.78, 2.53 (2d, ^2J = 14.4 Hz, 2H-3); 2.17 (br.s, H(OH)); 1.18–1.05 (m, 21H(TIPS)). ^{13}C NMR ($CDCl_3$, 100.6 MHz): 202.3 (s, C4); 137.0 (s, Car); 128.5 (d, ^1J = 161 Hz, 2CHar); 127.9 (d, ^1J = 161 Hz, CHar); 127.8 (d, ^1J = 158 Hz, 2CHar); 79.6 (s, C2); 76.9 (d, ^1J = 149 Hz, C6); 73.6 (t, ^1J = 142 Hz, CH_2(Bn)); 73.2 (t, ^1J = 142 Hz, CH_2-C2); 66.6 (t, ^1J = 145 Hz, CH_2-C2); 63.2 (t, ^1J = 144 Hz, CH_2-C6); 62.8 (d, ^1J = 141 Hz, C5); 43.0 (t, ^1J = 145 Hz, C3); 17.9 (q, ^1J = 126 Hz, 6Me(TIPS)); 11.9 (d, ^1J = 117 Hz, 3CH(TIPS)). CI-MS(NH_3): m/z 495 (7, $[M+NH_4]^+$), 450 (2, $[M+H-N_2]^+$), 406 (2, $[M-N_2-i\text{-Pr}]^+$), 358 (10, $[M-N_2-Bn]^+$), 296 (4), 203 (4), 161 (7), 91 (80), 75 (100).

*4.8. (2*RS*,5*SR*,6*RS*)-2-[(Acetyloxy)methyl]-5-azido-2-[(benzyloxy)methyl]-2,3,5,6-tetrahydro-6-{[(triisopropylsilyl)oxy]methyl}-4*H*-pyran-4-one (±)-**11**

Ac_2O (60 mL) was added to a soln of pure (±)-**10** (7.07 g, 14.8 mmol) in pyridine (60 mL) stirred at 0°C. After 1 h, the reaction was treated with Et_2O (200 mL) and 1N HCl (50 mL). The aq. phase was extracted with Et_2O (200 mL, four times). The combined org. extracts were washed with a sat. aq. soln of $NaHCO_3$ (until neutrality of aq. phase), dried ($MgSO_4$) and concentrated. The residual pyridine was evaporated under reduced pressure to afford a light yellow oil (7.3 g, 95%). An analytical sample of (±)-**11** can be obtained by FC on silica gel (light petroleum ether/EtOAc (4:1) (R_f (light petroleum ether/EtOAc (3:1)) = 0.40)): colorless oil. UV (CH_3CN): λ_{max} = 208 nm (ε = 6700 [dm^3 cm^{-1} mol^{-1}]). IR (film): 3440, 2960, 2865, 2115, 1730, 1650, 1455, 1380, 1365, 1240, 1145, 1100, 1050, 995, 885, 735, 700 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): 7.39–7.23 (m, 5H(Ph)); 4.48 (s, CH_2(Bn)); 4.19 (br.d, ^3J(H-5,H-6) = 9.5 Hz, H-5); 4.06, 4.00 (2d, ^2J = 11.2 Hz, $BnOCH_2$-C2); 4.01 (ddd, ^3J(H-6,H-5) = 9.5 Hz, ^3J = 2.9 Hz, ^3J = 1.4 Hz, H-6); 3.97 (dd, ^2J = 11.5 Hz, ^3J = 1.4 Hz, H-C-C6); 3.89 (dd, ^2J = 11.5 Hz, ^3J = 2.9 Hz, H′-C-C6); 3.58, 3.47 (2d, ^2J = 10.4 Hz, $AcOCH_2$-C2); 2.62 (d, ^2J = 14.9 Hz, H-3); 2.50 (dd, ^2J = 14.9 Hz, ^4J(H′-3,H-5) = 0.9 Hz, H′-3); 2.02 (s, Me(Ac)); 1.20–1.00 (m, 21H(TIPS)). ^{13}C NMR ($CDCl_3$, 100.6 MHz): 201.6 (s, C4); 170.3 (s, C=O(Ac)); 136.9 (s, Car); 128.5 (d, ^1J = 161 Hz, 2CHar); 127.9 (d, ^1J = 161 Hz, CHar); 127.8 (d, ^1J = 158 Hz, 2CHar); 77.8 (s, C2); 76.7 (d, C6); 73.6 (t, ^1J = 141 Hz, CH_2(Bn)); 72.3 (t, ^1J = 142 Hz, CH_2-C2); 67.1 (t, ^1J = 149 Hz, CH_2-C2); 63.1 (t, ^1J = 143 Hz, CH_2-C6); 62.9 (d, ^1J = 139 Hz, C5); 44.0 (t, ^1J = 131 Hz, C3); 20.6 (q, ^1J = 130 Hz, Me(Ac)); 17.9 (q, ^1J = 126 Hz, 6Me(TIPS)); 11.9 (d, ^1J = 121 Hz, 3CH(TIPS)). CI-MS(NH_3): m/z 537 (42, $[M+NH_4]^+$), 492 (12, $[M+H-N_2]^+$), 476 (17, $[M-i\text{-Pr}]^+$), 448 (15, $[M-i\text{-Pr}-N_2]^+$), 91 (100). Anal. calcd for $C_{26}H_{41}N_3O_6Si$ (519.72): C, 60.09; H, 7.95; N, 8.09; Si, 5.40. Found: C, 60.18; H, 7.89; N, 8.11; Si, 5.32.

*4.9. (2RS,4RS,5RS,6RS)-5-Azido-2-[(benzyloxy)methyl]-4-hydroxy-3,4,5,6-tetrahydro-6-{[(triisopropylsilyl)oxy]methyl}-2H-pyran-2-methanol acetate ((±)-**12**) and (2RS,4SR,5RS,6RS)-5-azido-2-[(benzyloxy)methyl]-4-hydroxy-3,4,5,6-tetrahydro-6-{[(triisopropylsilyl)oxy]methyl}-2H-pyran-2-methanol acetate (±)-**13***

$NaBH_4$ (638 mg, 16.9 mmol) was added portionwise to a soln of crude (±)-**11** (7.3 g, 14 mmol) in MeOH (100 mL) stirred at 0°C. After 30 min, the soln was diluted with EtOAc (100 mL), 1N HCl (50 mL) and the solvents were evaporated. The aq. phase was extracted with EtOAc (200 mL, four times). The combined org. layers were washed with a sat. aq. soln of $NaHCO_3$ (50 mL, two times), dried ($MgSO_4$) and concentrated to afford 7.65 g of a 14.4:1 mixture of (±)-**12** and (R_f (light petroleum ether/AcOEt (2:1)) = 0.42) and (±)-**13** (R_f (light petroleum ether/AcOEt (2:1)) = 0.30). Data for (±)-**12**. Mp: 84–86°C. UV (CH_3CN): λ_{max} = 262 nm (ε = 1400 [dm^3 cm^{-1} mol^{-1}]), 208 (8200). IR (KBr): 3430, 2945, 2865, 2105, 1735, 1465, 1385, 1245, 1135, 1095, 1050, 1025, 995, 915, 885, 850, 755, 700 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): 7.38–7.28 (m, 5H(Ph)); 4.59, 4.54 (2d, ^2J = 12.1 Hz, CH_2(Bn)); 4.24 (ddd, ^3J(H-4,H-3) = 3.6 Hz, ^3J(H-4,H-3) = 3.0 Hz, ^3J(H-4,H-5) = 3.0 Hz, H-4); 4.01, 3.97 (2d, ^2J = 11.2 Hz, CH_2-C2); 3.93–3.91 (m, CH_2-C6); 3.84 (ddd, ^3J(H-6,H-5) = 10.0 Hz, ^3J = 2.4 Hz, ^3J = 2.4 Hz, H-6); 3.74, 3.71 (2d, ^2J = 10.0 Hz, CH_2-C2); 3.67 (dd, ^3J(H-5,H-6) = 10.0 Hz, ^3J(H-5,H-4) = 3.0 Hz, H-5); 2.85 (br.s, H(OH)); 2.06 (dd, ^2J = 14.8 Hz, ^3J(H-3,H-4) = 3.0 Hz, H-3); 2.00 (s, Me(Ac)); 1.74 (dd, ^2J = 14.8 Hz, ^3J(H′-3,H-4) = 3.6 Hz, H′-3); 1.11–1.05 (m, 21H(TIPS)). ^{13}C NMR ($CDCl_3$, 100.6 MHz): 170.7 (s, C=O(Ac)); 137.6 (s, C4); 128.4 (d, ^1J = 160 Hz, 2CHar); 127.8 (d, ^1J = 159 Hz, CHar); 127.8 (d, ^1J = 160 Hz, 2CHar); 73.7 (s, C2); 73.5 (t, ^1J = 143 Hz, CH_2(Bn)); 70.5 (t, ^1J = 145 Hz, CH_2-C2); 69.7 (d, ^1J = 141 Hz, C6); 68.5 (t, ^1J = 150 Hz, CH_2-C2); 66.2 (d, ^1J = 153 Hz, C4); 63.7 (t, ^1J = 144 Hz, CH_2-C6); 60.1 (d, ^1J = 145 Hz, C5); 33.4 (t, ^1J = 127 Hz, C3); 20.8 (q, ^1J = 129 Hz, Me(Ac)); 17.9 (q, ^1J = 127 Hz, 6Me(TIPS)); 11.9 (d, ^1J = 119 Hz, 3CH(TIPS)). CI-MS(NH_3): *m*/*z* 539 (10, $[M+NH_4]^+$), 478 (9), 91 (100). Anal. calcd for $C_{26}H_{43}N_3O_6Si$ (521.74): C, 59.86; H, 8.31. Found: C, 59.72; H, 8.17.

*4.10. (2RS,4RS,5SR,6RS)-5-Azido-2-[(benzyloxy)methyl]-3,4,5,6-tetrahydro-4-[(triethylsilyl)-oxy]-6-{[(triisopropylsilyl)oxy]methyl}-2H-pyran-2-methanol acetate (±)-**14***

Et_3SiCl (3 mL, 17.6 mmol) was added dropwise to a soln of crude (±)-**12** (7.65 g) and imidazole (2.4 g, 35.1 mmol) in DMF (60 mL) stirred at 0°C. At the end of addition, the reaction was allowed to warm to 20°C. After stirring for 20 h at 20°C, the mixture was treated with Et_2O (200 mL), and brine (50 mL). The aq. phase was extracted with Et_2O (200 mL, five times). The combined org. layers were washed with a sat. aq. soln of $NaHCO_3$ (100 mL, two times), dried ($MgSO_4$), and concentrated. The residual DMF was evaporated under reduced pressure. FC (silica gel, light petroleum ether/EtOAc (4:1)) afforded (±)-**14** (8.24 g) as a colorless oil, contaminated by some Et_3SiOH ((±)-**14**/Et_3SiOH = 2:1). Converted yield: 78% of pure (±)-**14** based on (±)-**10**. UV (CH_3CN): λ_{max} = 273 nm (ε = 1500 [dm^3 cm^{-1} mol^{-1}]), 224 (3900). IR (film): 2945, 2865, 2105, 1745, 1455, 1380, 1240, 1135, 1095, 1070, 1000, 885, 785, 735 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): 7.36–7.25 (m, 5H(Ph)); 4.57, 4.47 (2d, ^2J = 12.1 Hz, CH_2(Bn)); 4.28 (ddd, ^3J(H-4,H-3) = 3.9 Hz, ^3J(H-4,H-3) = 3.6 Hz, ^3J(H-4,H-5) = 3.0 Hz, H-4); 4.05 (s, CH_2-C2); 3.92–3.89 (m, CH_2-C6); 3.83, 3.66 (2d, ^2J = 10.0 Hz, CH_2-C2); 3.80 (ddd, ^3J(H-6,H-5) = 9.7 Hz, ^3J = 2.4 Hz, ^3J = 2.4 Hz, H-6); 3.44 (dd, ^3J(H-5,H-6) = 9.7 Hz, ^3J(H-5,H-4) = 3.0 Hz, H-5); 1.99 (s, Me(Ac)); 1.89 (dd, ^2J = 14.2 Hz, ^3J(H-3,H-4) = 3.9 Hz, H-3); 1.63 (dd, ^2J = 14.2 Hz, ^3J(H′-

3,H-4)=3.6 Hz, H′-3); 1.11–1.06 (m, 21H(TIPS)); 0.97 (t, ^3J=7.9 Hz, 3Me(TES)); 0.65 (q, ^3J=7.9 Hz, 3CH_2(TES)). ^{13}C NMR ($CDCl_3$, 100.6 MHz): 170.7 (s, C=O(Ac)); 138.3 (s, Car); 128.2 (d, ^1J=160 Hz, 2CHar); 127.6 (d, ^1J=158 Hz, 2CHar); 127.5 (d, ^1J=160 Hz, CHar); 74.2 (s, C2); 73.2 (t, ^1J=142 Hz, CH_2(Bn)); 69.1 (d, ^1J=143 Hz, C6); 68.5 (t, ^1J=145 Hz, CH_2-C2); 67.9 (t, ^1J=150 Hz, CH_2-C2); 67.8 (d, ^1J=147 Hz, C4); 63.9 (t, ^1J=144 Hz, CH_2-C6); 59.6 (d, ^1J=144 Hz, C5); 34.4 (t, ^1J=126 Hz, C3); 20.8 (q, ^1J=129 Hz, Me(Ac)); 17.9 (q, ^1J=126 Hz, 6Me(TIPS)); 11.9 (d, ^1J=117 Hz, 3CH(TIPS)); 6.8 (q, ^1J=126 Hz, 3Me(TES)); 4.7 (d, ^1J=117 Hz, 3CH_2(TES)). CI-MS(NH_3): *m*/*z* 653 (14, $[M+NH_4]^+$), 608 (5, $[M+H-N_2]^+$), 592 (5), 578 (2), 564 (3), 91 (100). Anal. calcd for $C_{32}H_{57}N_3O_6Si_2$ (636.00): C, 60.43; H, 9.03. Found: C, 60.51; H, 9.02.

*4.11. (2*RS,*4*SR,*5*RS,*6*SR*)-5-Azido-2-[(benzyloxy)methyl]-3,4,5,6-tetrahydro-4-[(triethylsilyl)-oxy]-6-{[(triisopropylsilyl)oxy]methyl}-2*H*-pyran-2-methanol (±)-**15**

Anh. K_2CO_3 (5.13 g, 37.1 mmol) was added to a soln of pure (±)-**14** (4.72 g, 7.42 mmol) in MeOH (75 mL) stirred at 20°C. After 40 min, the soln was treated with a sat. aq. soln of $NaHCO_3$ (30 mL) and the methanol was evaporated. The aq. phase was extracted with EtOAc (200 mL, three times). The combined org. extracts were washed with a sat. aq. soln of $NaHCO_3$ (30 mL), dried ($MgSO_4$) and concentrated: light yellow oil (4.22 g, 96%). An analytical sample of (±)-**15** (colorless oil) can be obtained by FC (silica gel, EtOAc/light petroleum ether (1:4), R_f=0.42). UV (CH_3CN): λ_{max}=260 nm (ε=2300 [dm^3 cm^{-1} mol^{-1}]), 257 nm (2400), 212 nm (7100). IR (film): 3455, 2955, 2870, 2105, 1465, 1415, 1385, 1365, 1255, 1125, 1095, 1065, 1015, 995, 885, 785, 740 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): 7.40–7.26 (m, 5H(Ph)); 4.58, 4.48 (2d, ^2J=12.1 Hz, CH_2(Bn)); 4.32 (ddd, ^3J(H-4,H-3)=3.7 Hz, ^3J(H-4,H-3)=3.2 Hz, ^3J(H-4,H-5)=2.9 Hz, H-4); 3.96 (dd, ^2J=11.1 Hz, ^3J=2.9 Hz, H-C-C6); 3.91 (dd, ^2J=11.1 Hz, ^3J=2.0 Hz, H′-C-C6); 3.85 (ddd, ^3J(H-6,H-5)=9.8 Hz, ^3J=2.9 Hz, ^3J=2.0 Hz, H-6); 3.80, 3.76 (2d, ^2J=9.5 Hz, CH_2-C2); 3.63, 3.44 (2d, ^2J=11.2 Hz, CH_2-C2); 3.40 (dd, ^3J(H-5,H-4)=9.8 Hz, ^3J(H-5,H-4)=2.9 Hz, H-5); 2.15 (br.s, H(OH)); 1.92 (dd, ^2J=14.4 Hz, ^3J(H-3,H-4)=3.7 Hz, H-3); 1.85 (dd, ^2J=14.4 Hz, ^3J(H′-3,H-4)=3.2 Hz, H′-3); 1.19–1.06 (m, 21H(TIPS)); 0.99 (t, ^3J=7.9 Hz, 3Me(TES)); 0.65 (q, ^3J=7.9 Hz, 3CH_2(TES)). ^{13}C NMR ($CDCl_3$, 100.6 MHz): 138.3 (s, Car); 128.3 (d, ^1J=160 Hz, 2CHar); 127.6 (d, ^1J=161 Hz, 2CHar); 127.5 (d, ^1J=161 Hz, CHar); 75.1 (s, C2); 73.4 (t, ^1J=142 Hz, CH_2(Bn)); 70.5 (t, ^1J=143 Hz, CH_2-C2); 69.0 (d, ^1J=143 Hz, C6); 68.0 (d, ^1J=146 Hz, C4); 67.9 (t, ^1J=145 Hz, CH_2-C2); 63.8 (t, ^1J=141 Hz, CH_2-C6); 59.5 (d, ^1J=144 Hz, C5); 33.5 (t, ^1J=129 Hz, C3); 17.9 (q, ^1J=126 Hz, 6Me(TIPS); 11.9 (d, ^1J=117 Hz, 3CH(TIPS)); 6.8 (q, ^1J=126 Hz, 3Me(TES)); 4.7 (d, ^1J=117 Hz, 3CH_2(TES)). CI-MS(NH_3): *m*/*z* 611 (12, $[M+NH_4]^+$), 594 (2, $[M+H]^+$), 566 (4, $[M+H-N_2]^+$), 550 (2, $[M-i\text{-}Pr]^+$), 536 (2, $[M-N_2-Et]^+$), 522 (8, $[M-i\text{-}Pr-N_2]^+$), 91 (100). Anal. calcd for $C_{30}H_{55}N_3O_5Si_2$ (593.96): C, 60.67; H, 9.34; N, 7.08; Si, 9.45. Found: C, 60.64; H, 9.23; N, 6.93; Si, 9.32.

*4.12. (2*RS,*4*RS,*5*SR,*6*RS*)-5-Azido-2-[(benzyloxy)methyl]-3,4,5,6-tetrahydro-4-[(triethylsilyl)-oxy]-6-{[(triisopropylsilyl)oxy]methyl}-2*H*-pyran-2-carboxaldehyde and ((2*RS,*4*RS,*5*SR,*6*RS*)-2,6-anhydro-5-azido-2-*C*-[(benzyloxy)methyl]-3,5-dideoxy-4-*O*-triethylsilyl-7-*O*-triisopropylsilyl-DL*-allo-heptose (±)-**3**

1,1,1-Triacetoxy-1,1-dihydro-1,2-benziodoxol-3(1*H*)-one (Dess–Martin periodinane) (4.72 g, 11.1 mmol) was added to a soln of crude (±)-**15** (4.22 g, 7.10 mmol) in CH_2Cl_2 (75 mL) stirred

at 20°C. After stirring for 60 min, the reaction was diluted with CH_2Cl_2 (50 mL) and a 1 M aq. soln of $Na_2S_2O_3$ (30 mL). The aq. soln was extracted with CH_2Cl_2 (200 mL, three times). The combined org. extracts were washed with a 1 M aq. soln of $Na_2S_2O_3$ (30 mL), dried ($MgSO_4$) and concentrated. The resulting white solid was filtered (3 cm pad of silica gel, EtOAc/light petroleum ether (1:4) as eluant) to eliminate most of residual Dess–Martin periodinane. Although aldehyde (±)-**3** is not very stable on silica gel, an analytical sample can be obtained by FC (silica gel, EtOAc/light petroleum ether (1:9), R_f (EtOAc/light petroleum ether (1:4)) = 0.65) to afford a colorless oil. UV (CH_3CN): $\lambda_{max} = 206$ nm ($\varepsilon = 9100$ [$dm^3\ cm^{-1}\ mol^{-1}$]). IR (film): 2955, 2685, 2105, 1740, 1465, 1415, 1365, 1300, 1260, 1135, 1100, 1070, 1030, 995, 885, 735 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): 9.61 (d, $J = 1.1$ Hz, H-1); 7.36–7.26 (m, 5H(Ph)); 4.55, 4.46 (2d, $^2J = 12.4$ Hz, CH_2(Bn)); 4.24–4.19 (m, H-4+1H of BnOCH_2-C2); 3.99–3.97 (m, 2H-7); 3.84 (ddd, ^3J(H-6,H-5) = 9.2 Hz, ^3J(H-6, H-7) = 2.8 Hz, ^3J(H-6,H-7) = 2.8 Hz, H-6); 3.56 (d, $^2J = 10.9$ Hz, 1H of BnOCH_2-C2); 3.48 (dd, ^3J(H-5,H-6) = 9.2 Hz, ^3J(H-5,H-4) = 2.9 Hz, H-5); 1.78 (dd, $^2J = 14.4$ Hz, ^3J(H-3,H-4) = 4.3 Hz, H-3); 1.65 (dd, $^2J = 14.4$ Hz, ^3J(H′-3,H-4) = 2.9 Hz, H′-3); 1.17–1.07 (m, 21H(TIPS)); 0.94 (t, $^3J = 7.8$ Hz, 3Me(TES)); 0.61 (q, $^3J = 7.8$ Hz, 3CH_2(TES)). ^{13}C NMR ($CDCl_3$, 100.6 MHz): 203.8 (d, $^1J = 183$ Hz, C1); 137.8 (s, Car); 128.2 (d, $^1J = 160$ Hz, 2CHar); 127.7 (d, $^1J = 160$ Hz, CHar); 127.7 (d, $^1J = 159$ Hz, 2CHar); 80.7 (s, C1); 73.5 (t, $^1J = 142$ Hz, CH_2(Bn)); 70.0 (t, $^1J = 142$ Hz, BnOCH_2-C2); 69.8 (d, $^1J = 145$ Hz, C6); 67.1 (d, $^1J = 146$ Hz, C4); 63.6 (t, $^1J = 143$ Hz, C7); 59.3 (d, $^1J = 142$ Hz, C5); 34.0 (t, $^1J = 129$ Hz, C3); 17.9 (q, $^1J = 126$ Hz, 6Me(TIPS)); 11.9 (d, $^1J = 117$ Hz, 3CH(TIPS)); 6.8 (q, $^1J = 126$ Hz, 3Me(TES)); 4.7 (d, $^1J = 116$ Hz, 3CH_2(TES)). CI-MS(NH_3): m/z 609 (99, $[M+NH_4]^+$), 592 (10, $[M+H]^+$, 10.2), 564 (27, $[M+H-N_2]^+$), 548 (20, $[M-i\text{-}Pr]^+$), 534 (16, $[M-N_2-Et]^+$), 520 (28, $[M-N_2-i\text{-}Pr]^+$), 91 (100). Anal. calcd for $C_{30}H_{53}N_3O_5Si_2$ (591.94): C, 60.87; H, 9.02; N, 7.10; O, 13.51. Found: C, 60.93; H, 9.15; N, 7.01; O, 13.47.

*4.13. (2*R*,4*R*,5*S*,6*R*)-2,6-Anhydro-5-azido-2-*C*-[(benzyloxy)methyl]-3,5-dideoxy-4-*O*-triethylsilyl-7-*O*-triisopropylsilyl-L-*allo*-heptose (−)-**3**

Compound (−)-**16** (2.07 g, 2.63 mmol) was dissolved in Et_2O (100 mL) and extracted with 1N HCl (20 mL, three times). The org. phase was washed with a sat. aq. soln of $NaHCO_3$ (until neutrality), dried ($MgSO_4$) and concentrated to afford (−)-**3** (1.48g, 95%): colorless oil. Addition of $NaHCO_3$ to the aq. phase and extraction with CH_2Cl_2 (100 mL, three times), drying ($MgSO_4$) and concentration allowed recovery of the chiral diamine (507 mg, 91%). $[\alpha]^{25}_{589} = -51$, $[\alpha]^{25}_{577} = -53$, $[\alpha]^{25}_{546} = -60$, $[\alpha]^{25}_{435} = -109$, $[\alpha]^{25}_{403} = -135$ ($c = 1.0$, $CHCl_3$).

*4.14. (4*R*,5*R*)-2-{(2*S*,4*R*,5*S*,6*R*)-5-Azido-2-[(benzyloxy)methyl]-3,4,5,6-tetrahydro-4-[(triethylsilyl)oxy]-6-{[(triisopropylsilyl)oxy]methyl}-2*H*-pyran-2-yl}-4,5-diphenylimidazolidine ((−)-**16**) and (4*R*,5*R*)-2-{(2*R*,4*S*,5*R*,6*S*)-5-azido-2-[(benzyloxy)methyl]-3,4,5,6-tetrahydro-4-[(triethylsilyl)oxy]-6-{[(triisopropylsilyl)oxy]methyl}-2*H*-pyran-2-yl}-4,5-diphenylimidazolidine (+)-**17**

(1*R*,2*R*)-(+)-1,2-Diphenylethylenediamine (1.89 g, 8.90 mmol) was added to a soln of crude (±)-**3** (4.39 g) and 4 Å molecular sieves (4 g) in CH_2Cl_2 (75 mL) stirred at 20°C. After 22 h, the mixture was diluted with CH_2Cl_2 (100 mL), Et_3N (10 mL) and a sat. aq. soln of $NaHCO_3$ (50 mL). The aq. phase was extracted with CH_2Cl_2 (100 mL, four times). The combined org. extracts were washed with a sat. aq. soln of $NaHCO_3$ (50 mL), dried ($MgSO_4$) and concen-

trated. FC (silica gel, EtOAc/light petroleum ether (1:9)+1% NEt_3) afforded (−)-**16** (604 mg) and a mixture of (−)-**16** and (+)-**17** (3.88 g). (Overall yield based on (±)-**14**: 77%.) Analytical samples of (−)-**16** and (+)-**17** can be obtained by FC (silica gel, EtOAc/light petroleum ether (1:9)+1% NEt_3), R_f (EtOAc/light petroleum ether (1:3)) (−)-**16** = 0.38, R_f (EtOAc/light petroleum ether (1:3)) (+)-**17** = 0.47: colorless oils.

Data for (−)-**16**. $[\alpha]_{589}^{25} = -30$, $[\alpha]_{577}^{25} = -31$, $[\alpha]_{546}^{25} = -35$, $[\alpha]_{435}^{25} = -55$, $[\alpha]_{403}^{25} = -63$ ($c = 1.0$, $CHCl_3$). UV (CH_3CN): $\lambda_{max} = 213$ nm ($\varepsilon = 12700$ [dm^3 cm^{-1} mol^{-1}]). IR (film): 2955, 2870, 2105, 1495, 1455, 1415, 1380, 1295, 1255, 1115, 1015, 885, 785, 735, 700 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): 7.42–7.09 (m, 15H(Ph)); 4.82 (s, H-2); 4.59, 4.55 (2d, $^2J = 11.9$ Hz, CH_2(Bn)); 4.28, 4.14 (2d, $^2J = 9.3$ Hz, CH_2-C2′); 4.25 (d, ^3J(H-4,H-5) = 7.7 Hz, H-4); 4.20–4.16 (m, H-4′+H-5); 4.06 (ddd, ^3J(H-6′,H-5′) = 9.9 Hz, $^3J = 2.8$ Hz, $^3J = 1.9$ Hz, H-6′); 4.02 (dd, $^2J = 11.1$ Hz, $^3J = 2.8$ Hz, H-C-C6′); 3.95 (dd, $^2J = 11.1$ Hz, $^3J = 1.9$ Hz, H′-C-C6′); 3.56 (dd, ^3J(H-5′,H-6′) = 9.9 Hz, ^3J(H-5′,H-4′) = 2.8 Hz, H-5′); 2.37 (dd, $^2J = 14.5$ Hz, ^3J(H-3′,H-4′) = 3.1 Hz, H-3′); 2.18 (dd, $^2J = 14.5$ Hz, ^3J(H′-3′,H-4′) = 3.7 Hz, H′-3′); 1.21–1.15 (m, 21H(TIPS)); 1.11 (t, $^3J = 7.7$ Hz, 3Me(TES)); 0.76 (2q, $^3J = 7.7$ Hz, $3CH_2$(TES)). ^{13}C NMR ($CDCl_3$, 100.6 MHz): 142.9, 141.6, 138.7 (3s, 3Car); 128.4–127.1 (9d, $^1J \sim 160$ Hz, 15CHar); 78.6 (d, $^1J = 149$ Hz, C2); 76.6 (s, C2′); 73.5 (t, $^1J = 141$ Hz, CH_2(Bn)); 71.1 (d, $^1J = 139$ Hz, C5); 70.3 (t, $^1J = 145$ Hz, CH_2-C2′); 69.9 (d, $^1J = 143$ Hz, C4); 69.2 (d, $^1J = 142$ Hz, C6′); 68.4 (d, $^1J = 149$ Hz, C4′); 64.2 (t, $^1J = 141$ Hz, CH_2-C6′); 60.1 (d, $^1J = 142$ Hz, C5′); 33.0 (t, $^1J = 128$ Hz, C3′); 18.0 (q, $^1J = 126$ Hz, 6Me(TIPS)); 12.1 (d, $^1J = 118$ Hz, 3CH(TIPS)); 6.95 (q, $^1J = 126$ Hz, 3Me(TES)); 4.9 (d, $^1J = 117$ Hz, $3CH_2$(TES)). CI-MS(NH_3): m/z 786 (100, $[M+H]^+$), 757 (4, $[M-N_2]^+$), 742 (2, [M−*i*-Pr]$^+$), 681 (4), 636 (6), 609 (9),531(10), 223 (21).

Data for (+)-**17**. $[\alpha]_{589}^{25} = 42$, $[\alpha]_{577}^{25} = 43$, $[\alpha]_{546}^{25} = 49$, $[\alpha]_{435}^{25} = 85$, $[\alpha]_{403}^{25} = 105$ ($c = 1.0$, $CHCl_3$). UV (CH_3CN): $\lambda_{max} = 215$ nm ($\varepsilon = 13100$ [dm^3 cm^{-1} mol^{-1}]). IR (film): 2865, 2105, 1495, 1455, 1415, 1365, 1255, 1120, 1015, 885, 745, 700 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): 7.44–7.11 (m, 15H(Ph)); 4.84 (s, H-2); 4.62, 4.54 (2d, $^2J = 12.1$ Hz, CH_2(Bn)); 4.32, 4.04 (2d, $^2J = 9.8$ Hz, CH_2-C2′); 4.26 (d, ^3J(H-4,H-5) = 7.8 Hz, H-4); 4.18 (ddde, ^3J(H-4′,H-5′) = 4.0 Hz, ^3J(H-4′,H-3′) = 3.2 Hz, ^3J(H-4′,H-3′) = 2.9 Hz, H-4′); 4.26 (d, ^3J(H-5,H-4) = 7.8 Hz, H-5); 4.08 (dm, ^3J(H-6′,H-5′) = 9.8 Hz, H-6′); 4.01 (dd, $^2J = 10.9$ Hz, $^3J = 3.5$ Hz, H-C-C6′); 3.97 (dd, $^2J = 10.9$ Hz, $^3J = 2.5$ Hz, H-C-C6′); 3.43 (dd, ^3J(H-5′,H-6′) = 9.8 Hz, ^3J(H-5′,H-4′) = 2.9 Hz, H-5′); 2.50 (br.s, 2 NH); 2.23 (dd, $^2J = 14.4$ Hz, ^3J(H-3′,H-4′) = 3.2 Hz, H-3′); 2.17 (dd, $^2J = 14.4$ Hz, ^3J(H′-3′,H-4′) = 4.0 Hz, H′-3′); 1.21–1.15 (m, 21H(TIPS)); 1.13 (t, $^3J = 7.8$ Hz, 3Me(TES)); 0.78+0.77 (2q, $^3J = 7.8$ Hz, $3CH_2$(TES)). ^{13}C NMR ($CDCl_3$, 100.6 MHz): 142.9, 141.4, 138.7 (3s, 3Car); 128.3, 128.2, 128.0, 127.7, 127.5, 127.5, 127.3, 127.3, 127.1 (9d, $^1J \sim 160$ Hz, 15CHar); 78.0 (d, $^1J = 153$ Hz, C2); 77.2 (s, C2′); 73.5 (t, $^1J = 141$ Hz, CH_2(Bn)); 70.9 (d, $^1J = 135$ Hz, C5); 70.2 (t, $^1J = 145$ Hz, CH_2-C2′); 69.6 (d, $^1J = 138$ Hz, C4); 69.4 (d, $^1J = 138$ Hz, C6′); 68.5 (d, $^1J = 146$ Hz, C4′); 64.3 (t, $^1J = 141$ Hz, CH_2-C6′); 60.3 (d, $^1J = 144$ Hz, C5′); 32.9 (t, $^1J = 129$ Hz, C3′); 17.9 (q, $^1J = 126$ Hz, 6Me(TIPS)); 12.0 (d, $^1J = 118$ Hz, 3CH(TIPS)); 6.9 (q, $^1J = 126$ Hz, 3Me(TES)); 4.9 (d, $^1J = 117$ Hz, $3CH_2$(TES)). CI-MS(NH_3): m/z 786 (100, $[M+H]^+$), 758 (4, $[M+H-N_2]^+$), 742 (3, [M−*i*-Pr]$^+$), 635 (4, [M−CH_2OBn−Et]$^+$), 531 (6), 223 (42)).

*4.15. (1*R,*2*R,*5*R,*6*R,*7*R*)-6*-exo-*Azido-1-[(benzyloxy)methyl]-3,9-dioxabicyclo[3.3.1]nonan-2*-exo,*7*-exo-*diol (α-**18**) and (1*R,*2*S,*5*R,*6*R,*7*R*)-6*-exo-*azido-1-[(benzyloxy)methyl]-3,9-dioxabicyclo[3.3.1]nonan-2*-endo,*7*-exo-*diol β-**18***

HF/pyr (7:3) (1.4 mL, 52.2 mmol) was added to a soln of pure (−)-**16** (687 mg, 0.87 mmol) in THF (15 mL) stirred at 0°C. After 30 min, the mixture was treated with EtOAc (10 mL) and

a sat. aq. soln of $NaHCO_3$ (5 mL). The aq. phase was extracted with EtOAc (15 mL, three times). The combined org. extracts were washed with brine (10 mL), dried ($MgSO_4$) and concentrated. FC (silica gel, EtOAc/light petroleum ether (2:1), R_f (EtOAc) = 0.71) afforded a (1:2) mixture of α-**18**/β-**18** (208 mg, 75%). $[\alpha]_{589}^{25} = 45$, $[\alpha]_{577}^{25} = 49$, $[\alpha]_{546}^{25} = 54$, $[\alpha]_{435}^{25} = 97$, $[\alpha]_{403}^{25} = 120$ ($c = 0.5$, $CHCl_3$). UV (CH_3CN): $\lambda_{max} = 210$ nm ($\varepsilon = 6100$ [$dm^3\ cm^{-1}\ mol^{-1}$]). IR (film): 3420, 2920, 2100, 1705, 1495, 1455, 1360, 1265, 1160, 1095, 1020, 910, 880, 825, 735, 700 cm^{-1}. CI-MS(NH_3): m/z 339 (100, $[M+NH_4]^+$), 322 (19, $[M+H]^+$), 304 (36, $[M-OH]^+$), 294 (36, $[M+H-N_2]^+$), 276 (15, $[M-N_2-OH]^+$), 273 (17), 213 (17), 91 (32). Anal. calcd for $C_{15}H_{19}N_3O_5$ (321.33): C, 56.07; H, 5.96; N, 13.08. Found: C, 55.95; H, 6.09; N, 13.05. ^{1}H NMR ($CDCl_3$, 400 MHz) of α-**18**: 7.38–7.28 (m, 5H(Ph)); 4.90–4.76 (m, H-7+H-2); 4.56 (s, CH_2(Bn)); 4.38 (dd, $^2J = 12.4$ Hz, ^3J(H-4,H-5) = 4.0 Hz, H-4); 4.30–4.23 (m, HO-C2); 4.03 (m, H-5); 3.79–3.71 (m, H-6); 3.52, 3.40 (2d, $^2J = 9.9$ Hz, CH_2-C1); 3.40 (d, $^2J = 12.4$ Hz, H′-4); 2.42 (br.s, HO-C7); 2.00 (dd, $^2J = 13.6$ Hz, ^3J(H-8,H-7) = 6.1 Hz, H-8); 1.75 (dd, $^2J = 13.6$ Hz, ^3J(H′-8,H-7) = 11.2 Hz, H′-8). ^{13}C NMR ($CDCl_3$, 100.6 MHz) of α-**18**: 137.3 (s, Car); 128.4 (d, $^1J = 161$ Hz, 2CHar); 127.9 (d, $^1J = 161$ Hz, CHar); 127.7 (d, $^1J = 161$ Hz, 2CHar); 92.6 (d, $^1J = 169$ Hz, C2); 74.2 (s, C1); 73.9 (t, $^1J = 144$ Hz, CH_2(Bn)); 73.5 (t, $^1J = 144$ Hz, CH_2-C1); 71.0 (d, $^1J = 148$ Hz, C5); 64.3 (d, $^1J = 142$ Hz, C7); 64.1 (d, $^1J = 138$ Hz, C6); 58.5 (t, $^1J = 147$ Hz, C4); 35.2 (t, $^1J = 129$ Hz, C8). ^{1}H NMR ($CDCl_3$, 400 MHz) of β-**18**: 7.38–7.28 (m, 5H(Ph)); 5.01 (br.s, H-2); 4.20–4.16 (m, H-7); 4.63, 4.53 (2d, $^2J = 12.1$ Hz, CH_2(Bn)); 4.30–4.23 (m, HO-C2); 4.02 (dd, $^2J = 12.4$ Hz, ^3J(H-4,H-5) = 3.4 Hz, H-4); 3.96 (m, H-5); 3.79–3.71 (m, H-6+H′-4 where $^2J = 12.4$ Hz); 3.48, 3.38 (2d, $^2J = 10.5$ Hz, CH_2-C1); 2.58 (br.s, HO-C7); 2.15 (dd, $^2J = 13.3$ Hz, ^3J(H-8,H-7) = 5.9 Hz, H-8); 1.48 (dd, $^2J = 13.3$ Hz, ^3J(H′-8,H-7) = 5.9 Hz, H′-8). ^{13}C NMR ($CDCl_3$, 100.6 MHz) of β-**18**: 137.6 (s, Car); 128.4 (d, $^1J = 161$ Hz, 2CHar); 127.9 (d, $^1J = 161$ Hz, CHar); 127.7 (d, $^1J = 161$ Hz, 2CHar); 94.7 (d, $^1J = 166$ Hz, C2); 76.1 (s, C1); 73.9 (t, $^1J = 144$ Hz, CH_2(Bn)); 73.5 (t, $^1J = 142$ Hz, CH_2-C1); 70.8 (d, $^1J = 149$ Hz, C5); 65.9 (t, $^1J = 145$ Hz, C4); 64.5 (d, $^1J = 149$ Hz, C7); 63.6 (d, $^1J = 142$ Hz, C6); 30.8 (t, $^1J = 129$ Hz, C8).

*4.16. (1*R,*2*S,*5*R,*6*R,*7*R*)-6*-exo-*Azido-1-[(benzyloxy)methyl]-2*-endo-*methoxy-3,9-dioxabicyclo-[3.3.1]nonan-7*-exo-*ol (β-**19**) and (1*R,*2*R,*5*R,*6*R,*7*R*)-6*-exo-*azido-1-[(benzyloxy)methyl]-2*-exo-*methoxy-3,9-dioxabicyclo[3.3.1]nonan-7*-exo-*ol α-**19***

$SOCl_2$ (530 μL, 7.34 mmol) was added to a 1:2 soln of α-**18**/β-**18** (118 mg, 0.37 mmol) in MeOH (10 mL) stirred at 20°C. The mixture was stirred at 60°C for 24 h, then treated with Et_2O (50 mL) and a sat. aq. soln of $NaHCO_3$ (15 mL). The aq. phase was extracted with Et_2O (50 mL, three times). The combined org. extracts were washed with brine (20 mL), dried ($MgSO_4$) and concentrated. FC (silica gel, EtOAc/light petroleum ether (1:1), R_f (EtOAc) = 0.88): (1.7:1) mixture of α-**19**/β-**19** (87 mg, 71%). $[\alpha]_{589}^{25} = 43$, $[\alpha]_{577}^{25} = 43$, $[\alpha]_{546}^{25} = 45$, $[\alpha]_{435}^{25} = 72$, $[\alpha]_{403}^{25} = 95$ ($c = 0.3$, $CHCl_3$); UV (CH_3CN): $\lambda_{max} = 209$ nm ($\varepsilon = 5700$ [$dm^3\ cm^{-1}\ mol^{-1}$]). IR (film): 3480, 2935, 2120, 1455, 1355, 1270, 1070, 1020, 880, 830, 740, 700 cm^{-1}. CI-MS(NH_3): m/z 336 ($[M+H]^+$), 320 (36, $[M-Me]^+$), 307 (0.2, $[M-N_2]^+$), 304 (0.3, $[M-MeO]^+$), 276 (0.2, $[M-MeO-N_2]^+$), 258 (0.3, $[M-Ph]^+$), 200 (0.6, $[M-OBn-N_2]^+$), 134 (0.5), 91 (100); Anal. calcd for $C_{16}H_{21}N_3O_5$ (335.36): C, 57.29; H, 6.31; N, 12.53. Found: C, 57.34; H, 6.32; N, 12.54. ^{1}H NMR ($CDCl_3$, 400 MHz) of α-**19**: 7.38–7.26 (m, 5H(Ph)); 4.84–4.73 (m, H-7); 4.59, 4.46 (2d, $^2J = 12.1$ Hz, CH_2(Bn)); 4.375 (s, H-2); 4.20 (dd, $^2J = 12.1$ Hz, ^3J(H-4,H-5) = 3.8 Hz, H-4); 4.06–4.00 (m, H-5); 3.84–3.76 (m, H-6); 3.53, 3.34 (2d, $^2J = 9.2$ Hz, CH_2-C1); 3.47–3.405 (m, H′-4); 3.39 (s, 3H(MeO)); 2.22 (d, $^2J = 9.6$ Hz, OH); 2.13 (dd, $^2J = 13.7$ Hz, ^3J(H-8,H-7) = 5.9 Hz, H-8); 1.895

(dd, $^2J=13.7$ Hz, ^3J(H′-8,H-7)=11.4 Hz, H′-8). ^{13}C NMR ($CDCl_3$, 100.6 MHz) of α-**19**: 138.1 (s, Car); 128.2 (d, $^1J=159$ Hz, 2CHar); 127.7 (d, $^1J=159$ Hz, CHar); 127.7 (d, $^1J=159$ Hz, 2CHar); 98.5 (d, $^1J=168$ Hz, C2); 74.4 (s, C1); 73.6 (t, $^1J=146$ Hz, CH_2(Bn)); 73.5 (t, $^1J=145$ Hz, CH_2-C1); 70.8 (d, $^1J=148$ Hz, C5); 64.7 (d, $^1J=154$ Hz, C7); 64.4 (d, $^1J=143$ Hz, C6); 59.0 (t, $^1J=149$ Hz, C4); 55.3 (q, $^1J=144$ Hz, MeO); 35.8 (t, $^1J=131$ Hz, C8). ^{1}H NMR ($CDCl_3$, 400 MHz) of β-**19**: 7.38–7.26 (m, 5H(Ph)); 4.84–4.73 (m, H-7); 4.69 (s, H-2); 4.66, 4.50 (2d, $^2J=12.4$ Hz, CH_2(Bn)); 4.06–4.00 (m, H-5+H-4); 3.84–3.76 (m, H-6+ H′-4); 3.47–3.405 (m, 1H of CH_2-C1+3H(MeO)); 3.34 (d, $^2J=10.6$ Hz, 1H of CH_2-C1); 2.18 (d, $^2J=9.0$ Hz, OH); 2.04 (dd, $^2J=12.1$ Hz, ^3J(H-8,H-7)=6.0 Hz, H-8); 1.44 (dd, $^2J=12.1$ Hz, ^3J(H′-8,H-7)=12.1 Hz, H′-8). ^{13}C NMR ($CDCl_3$, 100.6 MHz) of β-**19**: 138.1 (s, Car); 128.2 (d, $^1J=159$ Hz, 2CHar); 127.7 (d, $^1J=159$ Hz, CHar); 127.7 (d, $^1J=159$ Hz, 2CHar); 101.1 (d, $^1J=164$ Hz, C2); 76.0 (s, C1); 73.6 (t, $^1J=141$ Hz, CH_2(Bn)); 73.1 (t, $^1J=143$ Hz, CH_2-C1); 71.1 (d, $^1J=148$ Hz, C5); 65.8 (t, $^1J=145$ Hz, C4); 64.6 (d, $^1J=153$ Hz, C7); 63.9 (d, $^1J=149$ Hz, C6); 56.8 (q, $^1J=145$ Hz, MeO); 31.6 (t, $^1J=133$ Hz, C8).

*4.17. (1*R,*2*S,*5*R,*6*R,*7*R*) 6*-exo-*Amino-1-[(benzyloxy)methyl]-2*-endo-*methoxy-3,9-dioxabicyclo-[3.3.1]nonan-7*-exo-*ol (β-**20**) and (1*R,*2*R,*5*R,*6*R,*7*R*) 6*-exo-*amino-1-[(benzyloxy)methyl]-2*-exo-*methoxy-3,9-dioxabicyclo[3.3.1]nonan-7*-exo-*ol α-**20***

Raney Ni (catalytic amount) was added to a (1.7:1) mixture of α-**19**/β-**19** (22 mg, 0.066 mmol) in EtOH. It was degassed and then pressurized with H_2 (1 atm) stirred at 20°C. After 90 min, the mixture was diluted with EtOH (10 mL) and filtered through a pad of Celite (2 cm). The Celite was washed with EtOH (10 mL, two times) and the solvents were evaporated: (1.7:1) mixture of α-**20**/β-**20** (17 mg, 83%). IR (film): 3425, 2935, 1455, 1360, 1245, 1210, 1070, 1025, 735, 700 cm^{-1}. CI-MS(NH_3): *m/z* 310 (7, $[M+H]^+$), 278 (12, $[M-OMe]^+$), 277 (19, $[M+H-OH-NH_2]^+$), 201 (9, $[M-Bn-OH]^+$), 169 (14, $[M-OBn-NH_2-OH]^+$), 91 (100, $[Bn]^+$). ^{1}H NMR ($CDCl_3$, 400 MHz) of α-**20**: 7.38–7.25 (m, 5H(Ph)); 4.66–4.44 (m, CH_2(Bn)+H-7); 4.34 (s, H-2); 4.17 (dd, $^2J=12.0$ Hz, ^3J(H-4,H-5)=2.8 Hz, H-4); 3.85–3.77 (m, H-5); 3.47–3.30 (m, CH_2-C1+ H′-4); 3.39 (s, 3H(MeO)); 3.02 (br.s, H-6); 2.57 (br.s, OH+NH_2); 2.05 (dd, $^2J=13.9$ Hz, ^3J(H-8,H-7)=6.2 Hz, H-8); 1.78 (dd, $^2J=13.9$ Hz, ^3J(H′-8,H-7)=12.0 Hz, H′-8). ^{13}C NMR ($CDCl_3$, 100.6 MHz) of α-**20**: 138.1 (s, Car); 128.3–127.5 (3*d*, 5CHar); 98.6 (d, C2); 74.2–73.4 (m, C1+CH_2(Bn)+CH_2-C1+C5); 62.9 (d, C7); 59.5 (t, C4); 55.1 (q, MeO); 53.0 (d, C6); 34.9 (t, C8). ^{1}H NMR ($CDCl_3$, 400 MHz) of β-**20**: 7.38–7.25 (m, 5H(Ph)); 4.66–4.44 (m, CH_2(Bn)+H-7+ H-2); 4.00 (br.d, $^2J=10.5$ Hz, H-4); 3.85–3.77 (m, H-5+H′-4); 3.47–3.30 (m, CH_2-C1); 3.44 (s, 3H(MeO)); 3.02 (br.s, H-6); 2.57 (br.s, OH+NH_2); 2.01 (dd, $^2J=13.9$ Hz, ^3J(H-8,H-7)=6.5 Hz, H-8); 1.28 (dd, $^2J=13.9$ Hz, ^3J(H′-8,H-7)=12.0 Hz, H′-8). ^{13}C NMR ($CDCl_3$, 100.6 MHz) of β-**20**: 137.9 (s, Car); 128.3–127.5 (3*d*, 5CHar); 101.3 (d, C2); 75.8 (s, C1); 74.2–73.4 (m, CH_2(Bn)+CH_2-C1+C5); 66.3 (t, C4); 62.9 (d, C7); 56.7 (q, MeO); 52.6 (d, C6); 30.8 (t, C8).

*4.18. (1*R,*2*R,*5*R,*6*R,*7*R*)-4-Methoxybenzoic acid 1-[(benzyloxy)methyl]-2*-exo-*methoxy-6-[(4-methoxybenzoyl)amino]-3,9-dioxabicyclo[3.3.1]nonan-7*-exo-*yl ester (β-**21**) and (1*R,*2*R,*5*R,*6*R,*7*R*)-4-methoxybenzoic acid 1-[(benzyloxy)methyl]-2*-exo-*methoxy-6-[(4-methoxybenzoyl)amino]-3,9-dioxabicyclo[3.3.1]nonan-7*-exo-*yl ester α-**21***

Paramethoxybenzoyl chloride (18.3 μL, 0.135 mmol) and DMAP (catalytic amount) were added to a (1.7:1) mixture of α-**20**/β-**20** (14 mg, 0.045 mmol) in pyridine (0.5 mL) stirred at

20°C. After stirring for 20 h, the mixture was treated with MeOH (1 mL) and H_2O (1 mL). The aq. phase was extracted with CH_2Cl_2 (5 mL, five times). The combined org. extracts were dried ($MgSO_4$) and concentrated. The residue was first chromatographed to eliminate *p*-methoxybenzoic acid and methyl *p*-methoxybenzoate. HPLC (EtOAc/light petroleum ether (3:2), Macherey–Nagel, Nuc 100-5, 6 mL/min, P = 48 bar): α-**21** (1.5 mg, 6%) and β-**21** (0.5 mg, 2%), colorless oils.

Data for α-**21**. (CH_3CN): $\lambda_{max} = 248$ nm ($\varepsilon = 15800$ [dm^3 cm^{-1} mol^{-1}]), 212 nm (12900). IR (film): 2925, 1705, 1650, 1605, 1495, 1455, 1260, 1170, 1100, 1075, 1030, 735 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): 7.88 (dm, $^3J = 9.0$ Hz, 2Har); 7.71 (dm, $^3J = 8.9$ Hz, 2Har); 7.38–7.31 (m, 5H(Ph)); 6.87 (dm, $^3J = 8.9$ Hz, 2Har); 6.82 (dm, $^3J = 9.0$ Hz, 2Har); 6.77 (d, ^3J(NH,H-6) = 9.1 Hz, NH); 6.15 (ddd, ^3J(H-7,H-8) = 11.3 Hz, ^3J(H-7,H-8) = 6.7 Hz, ^3J(H-7,H-6) = 5.1 Hz, H-7); 4.82 (ddd, ^3J(H-6,NH) = 9.1 Hz, ^3J(H-6,H-7) = 5.1 Hz, ^3J(H-6,H-5) = 1.9 Hz, H-6); 4.64, 4.52 (2d, $^2J = 11.9$ Hz, CH_2(Bn)); 4.48 (s, H-2); 4.26 (dd, $^2J = 12.3$ Hz, ^3J(H-4,H-5) = 3.9 Hz, H-4); 4.01 (m, H-5); 3.86 (s, MeO(PMBz)); 3.82 (s, MeO(PMBz)) 3.68 (d, $^2J = 12.3$ Hz, H-4); 3.53, 3.49 (2d, $^2J = 9.8$ Hz, CH_2-C1); 3.44 (s, 3H(MeO)); 2.30 (dd, $^2J = 14.1$ Hz, ^3J(H-8,H-7) = 6.7 Hz, H-8); 2.23 (dd, $^2J = 14.1$ Hz, ^3J(H′-8,H-7) = 11.3 Hz, H′-8). ^{13}C NMR ($CDCl_3$, 100.6 MHz): ~165 (4*s*, 4Car); 138.7 (s, Car); 131.7, 128.8, 128.4, 127.7, 127.5, 113.8, 113.5 (7d, 13CHar); 98.5 (d, C2); 77.2 (s, C1); 74.8, 73.8, 73.4 (2t+1d, CH_2(Bn)+CH_2-C1+C5); 72.4, 66.8, 59.1 (2d+1t, C7+C4+C6); 55.4, 55.3, 49.6 (3q, 3(MeO)); 31.3 (t, C8). CI-MS(NH_3): *m*/*z* 578 (100, $[M+H]^+$), 546 (6, $[M-OMe]^+$), 426 (2, $[M-PMBzO]^+$), 204 (3), 135 (11), 102 (4).

Data for β-**21**. UV (CH_3CN): $\lambda_{max} = 248$ nm ($\varepsilon = 17300$ [dm^3 cm^{-1} mol^{-1}]), 214 nm (13700). IR (film): 2925, 1645, 1605, 1495, 1455, 1375, 1255, 1170, 1095, 1025 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): 7.87 (dm, $^3J = 8.9$ Hz, 2Har); 7.69 (dm, $^3J = 9.0$ Hz, 2Har); 7.40–7.31 (m, 5H(Ph)); 6.89 (dm, $^3J = 9.0$ Hz, 2Har); 6.81 (dm, $^3J = 8.9$ Hz, 2Har); 6.72 (d, ^3J(NH,H-6) = 9.1 Hz, NH); 6.14 (ddd, ^3J(H-7,H-8) = 11.4 Hz, ^3J(H-7,H-8) = 6.3 Hz, ^3J(H-7,H-6) = 4.9 Hz, H-7); 4.81 (ddd, ^3J(H-6,NH) = 9.1 Hz, ^3J(H-6,H-7) = 4.9 Hz, ^3J(H-6,H-5) = 1.9 Hz, H-6)); 4.65, 4.57 (2d, $^2J = 12.1$ Hz, CH_2(Bn)); 4.63 (s, H-2); 4.01 (br.s, 2H-4); 4.01 (br.s, H-5); 3.86 (s, MeO(PMBz)); 3.82 (s, MeO(PMBz)); 3.53, 3.45 (2d, $^2J = 10.4$ Hz, CH_2-C1); 3.49 (s, 3H(MeO)); 2.35 (dd, $^2J = 13.2$ Hz, ^3J(H-8,H-7) = 6.3 Hz, H-8); 1.77 (dd, $^2J = 13.2$ Hz, ^3J(H′-8,H-7) = 11.4 Hz, H′-8)). ^{13}C NMR ($CDCl_3$, 100.6 MHz): ~165 (4*s*, 4Car); ~140 (s, Car); 131.7, 128.7, 128.4, 127.8, 127.7, 113.8, 113.5 (7d, 15CHar); 101.3 (d, C2); 77.2 (s, C1); 73.8, 73.0, 72.6 (2t+1d, CH_2(Bn)+CH_2-C1+C5); 66.5, 65.9, 57.9 (2d+1t, C7+C4+C6); 56.6, 55.4, 49.2 (3q, 3(MeO)); 27.5 (t, C8). CI-MS(NH_3): *m*/*z* 579 (100), 578 (99, $[M+1]^+$), 546 (1, $[M-OMe]^+$), 426 (5, $[M-PMBzO]^+$), 204 (3), 135 (14).

*4.19. (*R*)-α-Methoxy-α-(trifluoromethyl)benzylacetic acid (1*R*,2*R*,5*R*,6*R*,7*R*)-6-azido-1-[(benzyloxy)methyl]-2-*exo*-methoxy-3,9-dioxabicyclo[3.3.1]nonan-7-*exo*-yl ester ((*R*)-α-**22**) and (*R*)-α-methoxy-α-(trifluoromethyl)benzylacetic acid (1*R*,2*S*,5*R*,6*R*,7*R*)-6-azido-1-[(benzyloxy)-methyl]-2-*endo*-methoxy-3,9-dioxabicyclo[3.3.1]nonan-7-*exo*-yl ester(*R*)-β-**22***

(*S*)-(+)-α-Methoxy-α-(trifluoromethyl)-α-phenylacetyl chloride (34 μL, 0.18 mmol) and DMAP (catalytic amount) were added to a (1.7:1) soln of α-**19**/β-**19** (30 mg, 0.09 mmol) in pyridine (1 mL) stirred at 20°C. After 3 h 30 min, the mixture was treated with H_2O (1 mL). The aq. phase was extracted with Et_2O (10 mL, four times). The combined org. extracts were dried ($MgSO_4$) and concentrated. FC (silica gel, EtOAc/light petroleum ether (1:2), $R_f = 0.51$) afforded a (1.6:1) mixture of (*R*)-α-**22**/(*R*)-β-**22** (37 mg, 75%), colorless oil. $[\alpha]_{589}^{25} = 55$, $[\alpha]_{577}^{25} = 47$, $[\alpha]_{546}^{25} = 54$, $[\alpha]_{435}^{25} = 93$, $[\alpha]_{403}^{25} = 113$ ($c = 0.6$, $CHCl_3$). UV (CH_3CN): $\lambda_{max} = 213$ nm ($\varepsilon = 6600$ [dm^3 cm^{-1} mol^{-1}]). IR (film): 2935, 2865, 2105, 1750, 1495, 1455, 1355, 1260, 1185, 1170, 1125, 1095,

1075, 1020, 1000, 910, 825, 735, 700 cm^{-1}. CI-MS (NH_3): *m/z* 569 (100, $[M+NH_4]^+$), 524 (3, $[M+H-N_2]^+$), 520 (3.4, $[M-OMe]^+$), 189 (23), 156 (6), 91 (32). Anal. calcd for $C_{26}H_{28}F_3N_3O_7$ (551.52): C, 56.62; H, 5.12; N, 7.62. Found: C, 56.52; H, 5.24; N, 7.51. ^1H NMR ($CDCl_3$, 400 MHz) of (*R*) α-**22**: 7.63–7.27 (m, 10H(Ph)); 6.10–6.02 (m, H-7); 4.57, 4.44 (2d, $^2J=12.1$ Hz, CH_2(Bn)); 4.47 (s, H-2); 4.24 (dd, $^2J=12.3$ Hz, ^3J(H-4,H-5) = 3.7 Hz, H-4); 4.09–4.05 (m, H-5); 4.00–3.96 (m, H-6); 3.62 (br.s, 3H(MeO)); 3.55, 3.32 (2d, $^2J=9.1$ Hz, CH_2-C1); 3.51 (d, $^2J=12.3$ Hz, H′-4); 3.42 (s, 3H(MeO)); 2.16 (dd, $^2J=13.8$ Hz, ^3J(H-8,H-7) = 6.6 Hz, H-8); 2.11 (dd, $^2J=13.8$ Hz, ^3J(H′-8,H-7) = 11.3 Hz, H′-8). ^{13}C NMR ($CDCl_3$, 100.6 MHz) of (*R*)-α-**22**: 166.1 (s, COO); 137.9 (s, Car); 131.9 (s, Car); 129.7–127.3 (6*d*, $^1J=159$–162 Hz, 10CHar); 123.2 (q, $^1J_{C\text{-}F}=289$ Hz, CF_3); 98.3 (d, $^1J=169$ Hz, C2); 84.5 (s, *C*(Ph)(CF_3)(OMe)(COOR)); 74.4 (s, C1); 73.6 (t, $^1J=141$ Hz, CH_2(Bn)); 73.2 (t, $^1J=144$ Hz, CH_2-C1); 71.7 (d, $^1J=147$ Hz, C5); 70.5 (d, $^1J=155$ Hz, C7); 60.8 (d, $^1J=147$ Hz, C6); 58.8 (t, $^1J=148$ Hz, C4); 55.4 (2q, $^1J=143$ Hz, 2MeO); 31.3 (t, $^1J=133$ Hz, C8). ^1H NMR ($CDCl_3$, 400 MHz) of (*R*)-β-**22**: 7.63–7.27 (m, 10H(Ph)); 6.10–6.02 (m, H-7); 4.72 (s, H-2); 4.65, 4.50 (2d, $^2J=12.4$ Hz, CH_2(Bn)); 4.09–4.05 (m, H-5); 4.07, 3.90 (2d, $^2J=11.5$ Hz, 2H-4); 4.00–3.96 (m, H-6); 3.60 (br.s, 3H(MeO)); 3.48 (s, 3H(MeO)); 3.45, 3.34 (2d, $^2J=10.6$ Hz, CH_2-C1); 2.08 (dd, $^2J=13.5$ Hz, ^3J(H-8,H-7) = 6.8 Hz, H-8); 1.68 (dd, $^2J=13.5$ Hz, ^3J(H′-8,H-7) = 12.3 Hz, H′-8). ^{13}C NMR ($CDCl_3$, 100.6 MHz) of (*R*)-β-**22**: 165.9 (s, COO); 137.8 (s, Car); 131.9 (s, Car); 129.7–127.3 (6d, $^1J=159$–162 Hz, 10CHar); 123.2 (q, $^1J_{C\text{-}F}=289$ Hz, CF_3); 101.1 (d, $^1J=163$ Hz, C2); 84.8 (s, *C*(Ph)(CF_3)(OMe)(COOR)); 76.2 (s, C1); 73.7 (t, $^1J=141$ Hz, CH_2(Bn)); 72.7 (t, $^1J=142$ Hz, CH_2-C1); 71.9 (d, $^1J=149$ Hz, C5); 70.4 (d, $^1J=155$ Hz, C7); 65.7 (t, $^1J=145$ Hz, C4); 60.0 (d, $^1J=144$ Hz, C6); 56.8, 55.4 (2q, $^1J=143$ Hz, 2MeO); 27.0 (t, $^1J=133$ Hz, C8).

*4.20. (S)-α-Methoxy-α-(trifluoromethyl)benzylacetic acid (1R,2R,5R,6R,7R)-6-azido-1-[(benzyloxy)methyl]-2-*exo*-methoxy-3,9-dioxabicyclo[3.3.1]nonan-7-*exo*-yl ester ((S)-α-**22**) and (S)-α-methoxy-α-(trifluoromethyl)benzylacetic acid (1R,2S,5R,6R,7R)-6-azido-1-[(benzyloxy)-methyl]-2-*endo*-methoxy-3,9-dioxabicyclo[3.3.1]nonan-7-*exo*-yl ester (S)-β-**22***

Same procedure as above, starting from (*R*)-(−)-α-methoxy-α-(trifluoromethyl)-α-phenylacetyl chloride. It affords a 1.66:1 mixture of (*S*)-α-**22**/(*S*)-β-**22** (46 mg, 85%), colorless oil. $[\alpha]^{25}_{589}=-19$, $[\alpha]^{25}_{577}=-18$, $[\alpha]^{25}_{546}=-21$, $[\alpha]^{25}_{435}=-34$, $[\alpha]^{25}_{403}=-39$ ($c=0.34$, $CHCl_3$). UV (CH_3CN): $\lambda_{max}=209$ nm ($\varepsilon=10900$ [dm^3 cm^{-1} mol^{-1}]). IR (film): 2935, 2865, 2105, 1750, 1495, 1455, 1355, 1260, 1170, 1075, 1020, 915, 825, 735, 725, 620 cm^{-1}. CI-MS(NH_3): *m/z* 569 (100, $[M+NH_4]^+$), 524 (5, $[M+H-N_2]^+$), 520 (5, $[M-OMe]^+$), 189 (31), 156 (25), 91 (47). Anal. calcd for $C_{26}H_{28}F_3N_3O_7$ (551.52): C, 56.62; H, 5.12; N, 7.62. Found: C, 56.64; H, 5.17; N, 7.55. ^1H NMR ($CDCl_3$, 400 MHz) of (*S*)-α-**22**: 7.63–7.27 (m, 10H(Ph)); 6.12–6.04 (m, H-7); 4.59, 4.46 (2d, $^2J=12.1$ Hz, CH_2(Bn)); 4.48 (s, H-2); 4.22 (dd, $^2J=12.3$ Hz, ^3J(H-4,H-5) = 3.7 Hz, H-4); 4.09–4.02 (m, H-5); 3.90–3.86 (m, H-6); 3.61 (br.s, 3H(MeO)); 3.57, 3.35 (2d, $^2J=9.1$ Hz, CH_2-C1); 3.49 (d, $^2J=12.3$ Hz, H′-4); 3.42 (s, 3H(MeO)); 2.28 (dd, $^2J=13.5$ Hz, ^3J(H-8,H-7) = 6.3 Hz, H-8); 2.19 (dd, $^2J=13.5$ Hz, ^3J(H′-8,H-7) = 11.7 Hz, H′-8). ^{13}C NMR ($CDCl_3$, 100.6 MHz) of (*S*)-α-**22**: 166.0 (s, COO); 137.9 (s, Car); 131.9 (s, Car); 129.7–127.2 (6d, $^1J=159$–162, 10CHar); 123.2 (q, $^1J_{C\text{-}F}=289$ Hz, CF_3); 98.3 (d, $^1J=168$ Hz, C2); 84.4 (s, *C*(Ph)(CF_3)(OMe)(COOR)); 74.4 (s, C1); 73.6 (t, $^1J=142$ Hz, CH_2(Bn)); 73.2 (t, $^1J=145$ Hz, CH_2-C1); 71.7 (d, $^1J=148$ Hz, C5); 70.6 (d, $^1J=152$ Hz, C7); 60.9 (d, $^1J=142$ Hz, C6); 58.8 (t, $^1J=145$ Hz, C4); 55.5 (2q, $^1J=145$ Hz, 2MeO); 31.5 (t, $^1J=131$ Hz, C8). ^1H NMR ($CDCl_3$, 400 MHz) of (*S*)-β-**22**: 7.63–7.27 (m, 10H(Ph)); 6.12–6.04 (m, H-7); 4.72 (s, H-2); 4.66, 4.51 (2d, $^2J=12.4$ Hz, CH_2(Bn)); 4.09–4.02 (m,

H-5+H-4); 3.90–3.86 (m, H′-4+H-6); 3.60, 3.49 (2*s*, 6H(MeO)); 3.47, 3.36 (2d, $^2J=10.6$ Hz, CH_2-C1); 2.18 (dd, $^2J=12.9$ Hz, ^3J(H-8,H-7)=6.5 Hz, H-8); 1.76 (dd, $^2J=12.9$, ^3J(H′-8,H-7)=12.2 Hz, H′-8). ^{13}C NMR ($CDCl_3$, 100.6 MHz) of (*S*)-β-**22**: 165.8 (s, COO); 137.8 (s, Car); 131.9 (s, Car); 129.7–127.2 (6*d*, $^1J=159$–162 Hz, 10CHar); 123.2 (q, $^1J_{C\text{-}F}=289$ Hz, CF_3); 100.9 (d, $^1J=165$ Hz, C2); 84.7 (s, *C*(Ph)(CF_3)(OMe)(COOR)); 76.2 (s, C1); 73.7 (t, $^1J=141$ Hz, CH_2(Bn)); 72.7 (t, $^1J=144$ Hz, CH_2-C1); 71.9 (d, $^1J=150$ Hz, C5); 70.4 (d, $^1J=152$ Hz, C7); 65.7 (t, $^1J=145.0$, C4); 60.1 (d, $^1J=145$ Hz, C6); 56.8, 55.5 (2q, $^1J=144$ Hz, 2MeO); 27.2 (t, $^1J=132$ Hz, C8).

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