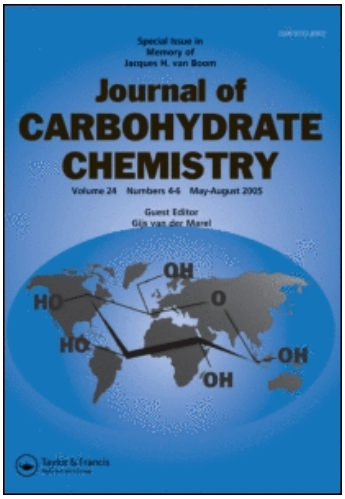

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Syntheses of Acyclo-*C*-nucleoside Analogs from 2,3:4,5-Di-*O*-isopropylidene-D-xylose

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Syntheses of Acyclo-*C*-nucleoside Analogs from 2,3:4,5-Di-*O*-isopropylidene-D-xylose

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Treatment of 1,2-dideoxy-4,5:6,7-di-*O*-isopropylidene-D-*xylo*-hept-1-yn-3-uloses **4a,b** with hydrazine hydrate and amidines yielded the 3-(1,2:3,4-di-*O*-isopropylidene-D-*xylo*-1,2,3,4-tetrahydroxy-butyl)-5-phenyl-1*H*(2*H*)-pyrazole **5** and the substituted 4-(1,2:3,4-di-*O*-isopropylidene-D-*xylo*-1,2,3,4-tetrahydroxy-butyl)pyrimidines **7a–f**, respectively. Reaction of **4a,b** with 2-amino-benzimidazol afforded the 2-(1,2:3,4-di-*O*-isopropylidene-D-*xylo*-1,2,3,4-tetrahydroxy-butyl)benzo[4,5]imidazo[1,2-*a*]pyrimidines **9a**,**b**. Compound **4a** and 5-amino-pyrazole-4-carbonic acid derivatives yielded the

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Dedicated to Professor Dr. András Lipták on the occasion of his 70th birthday.
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5-(1,2:3,4-di-*O*-isopropylidene-D-*xylo*-1,2,3,4-tetrahydroxy-butyl)pyrazolo[1,5-*a*]pyrimidines **11a–d**. Deprotection of pyrazole **5**, pyrimidine **7a**, and pyrazolo[1,5-*a*]pyrimidine **11b** yielded the acyclo-*C*-nucleosides **6**, **8**, and **12**, respectively.

Keywords Acyclo-*C*-nucleoside, Heptynuloses, D-Xylose, Pyrazoles, Pyrimidines, Beno[4,5]-imidazo[1,2-*a*]pyrimidines, Pyrazolo[1,5-*a*]pyrimidines

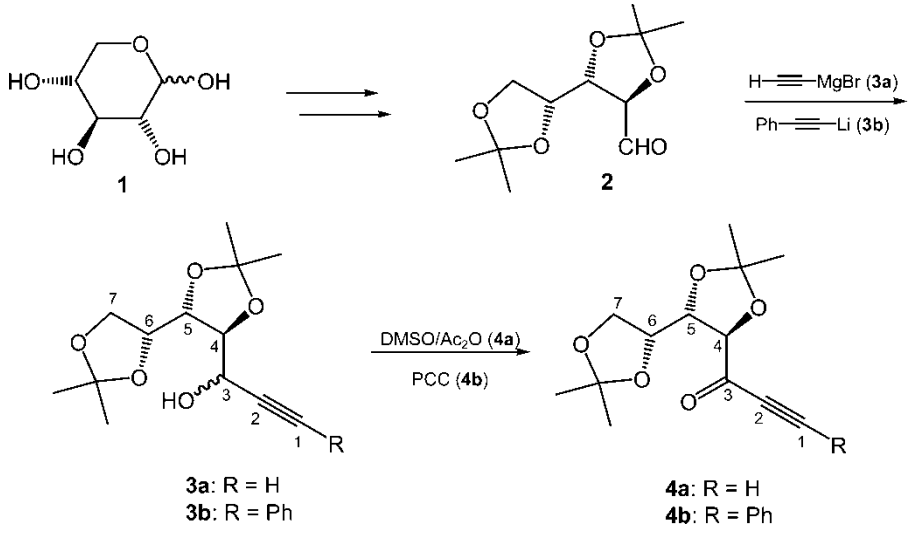
INTRODUCTION

In recent years the development of strategies for obtaining acyclo-*C*-nucleoside analogs has proved to be an active field of research.[1–5] In these analogs of nucleosides the furanose ring is replaced by a polyhydroxyalkyl chain and the heterocyclic units appear C,C-linked to these acyclic rests. The interest in acyclo-*C*-nucleosides has arisen due to the biologic and toxicologic properties displayed by many of these compounds. The natural products bengazol A and (−)-biopterin are representatives of biologically interesting acyclic *C*-nucleosides.[6,7] Natural as well as synthetic acyclic nucleoside analogs[8–12] have shown antiviral activities against herpes virus,[13] SIV,[14] and vaccinia.[15]

We chose to generate a reactive group within an acyclic carbohydrate derivative that would allow efficient construction of a range of heterocycles. Alkynyl ketones have been used in the formation of a range of heterocyclic systems. Pyrazoles, pyrimidines, pyridazines, pyridines, triazoles, and isoxazoles have all been prepared from these intermediates.[16,17] Using this approach, we recently reported the introduction of an alkynyl ketone functionality into the side chain of a monosaccharide to synthesize new iso-*C*-nucleosides.[18] Ethynyl ketones are valuable synthetic intermediates for the preparation of a wide range of simple nitrogen-containing heteroaromatic molecules and had been employed in the synthesis of heterocyclic building blocks, biologically active targets, non-proteinogenic amino acids, and pyrimidinyl-*C*-nucleosides.[19,20] In the present work the ynones **4a,b** synthesized from 2,3:4,5-di-*O*-isopropylidene-D-xylose represent a versatile class of compounds that can be used as starting materials for the synthesis of new acyclo-*C*-nucleosides.

RESULTS AND DISCUSSION

2,3:4,5-Di-*O*-isopropylidene-D-xylose **2** can be prepared starting from D-xylose in three reaction steps.[21,22] Treatment of **2** with a solution of ethynylmagnesium bromide or lithium phenylacetylide in THF resulted in the formation of the diastereomeric heptynols **3a**,**b**. The disappearance of the aldehyde signals and the new resonances for the alkyne carbon atoms in the ^{13}C NMR spectra clearly demonstrated the formation of the expected alcohols as (*R*,*S*)-mixtures. In the IR spectra absorption bands for the OH group and the triple bond were present (Scheme 1).



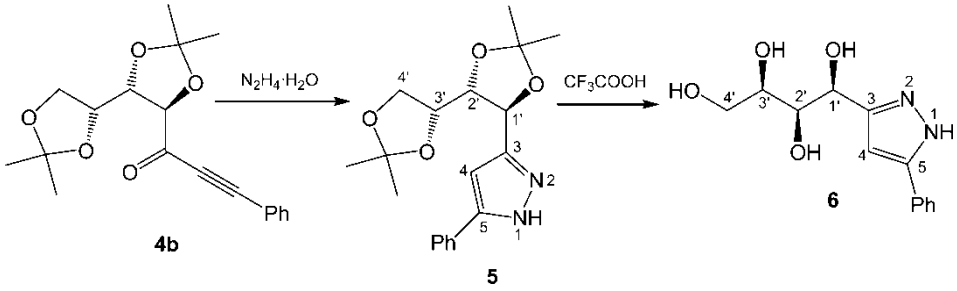
Scheme 1

Oxidation of heptynols **3a**,**b** afforded the desired hept-1-yn-3-uloses **4a**,**b**, which can be used in the facile synthesis of new acyclo-*C*-nucleosides. Heptynol **3b** was oxidized with PCC (pyridinium chlorochromate) in dichloromethane, yielding the ulose **4b** as a white solid in 52% yield. However, attempts to oxidize the heptynol **3a** with PCC, MnO_2, and other methods were unsuccessful. The synthesis of the 1,2-dideoxy-4,5:6,7-di-*O*-isopropylidene-D-*xylo*-hept-1-yn-3-ulose **4a** could only be achieved by using a mixture of dimethylsulfoxide and acetic acid anhydride.

Treatment of compound **4b** with hydrazine hydrate afforded the 3-(1,2:3,4-di-*O*-isopropylidene-D-*xylo*-1,2,3,4-tetrahydroxy-butyl)-5-phenyl-1*H*(2*H*)-pyrazole **5** in 85% yield. The heterocyclization could be confirmed by the absence of the signals for the carbonyl group and the disappearance of the triple bond in the ^{13}C NMR and the IR spectra. Generally, two tautomeric pyrazole structures could be formulated for the product. It is assumed that there is an equilibrium between the two tautomeric forms. Due to the fast NH-proton exchange process, the atoms C-3 and C-5 were not observable as separate signals in the ^{13}C NMR spectrum (Scheme 2).

In addition, we examined the deprotection of the synthesized compound. The cleavage of the isopropylidene groups of compounds **5** was successfully achieved with aqueous trifluoroacetic acid[23] at 70°C and afforded the acyclo-*C*-nucleoside analog **6** in 85% yield. In the ^{1}H NMR spectra, 6 signals for the isopropylidene groups were absent and four signals for OH groups were found instead.

Adamo et al.[16] had reported on the reaction of ynones with amidinium salts using ethyl acetate/water or acetonitrile as solvent and sodium carbonate as base to obtain the corresponding pyrimidines. Following this strategy, the



Scheme 2

ynones **4a**,**b** were allowed to react with acetamidinium chloride, benzamidinium chloride, *S*-methyl-isothiouronium sulfate, and *O*-methyl-isothiouronium hydrogensulfate to synthesize the pyrimidine acyclo-*C*-nucleosides **7a**–**f** in good yields. Compound **7f** was subjected to X-ray analysis at 173 K. The relevant crystallographic data are given in the experimental part. An ORTEP drawing of **7f** is shown in Figure 1, which gives the numbering

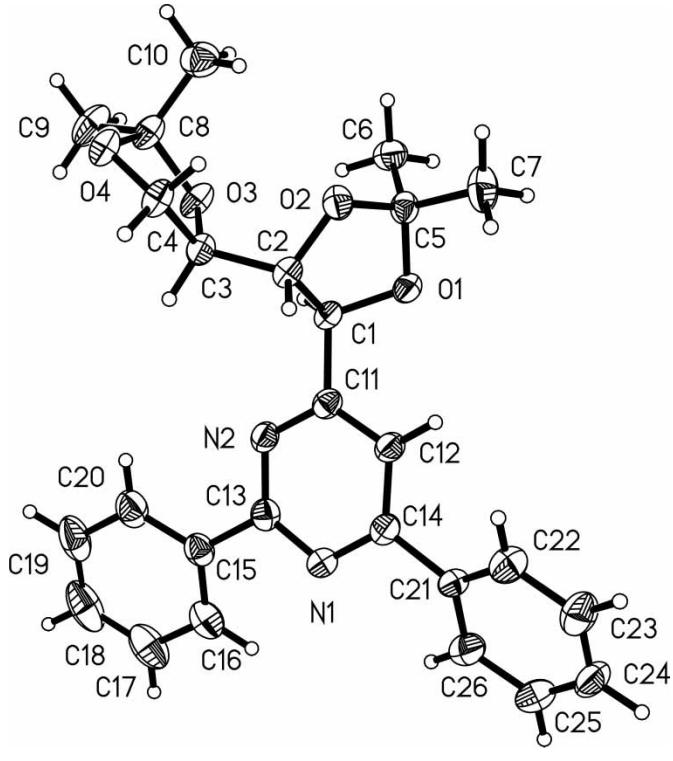
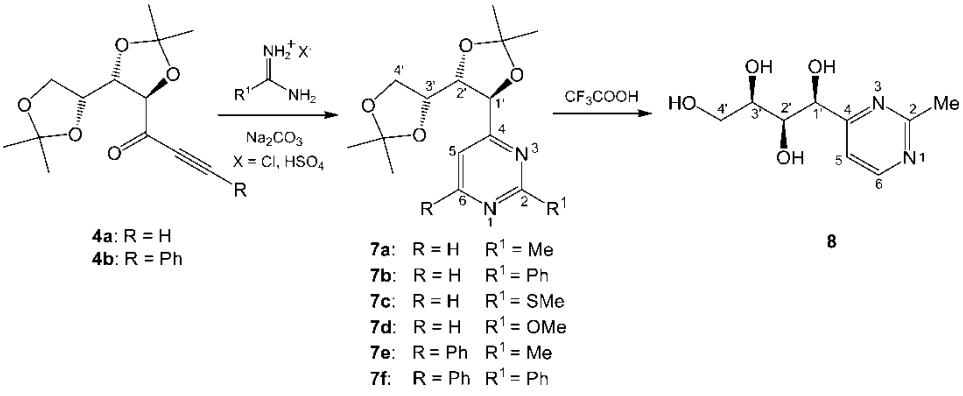


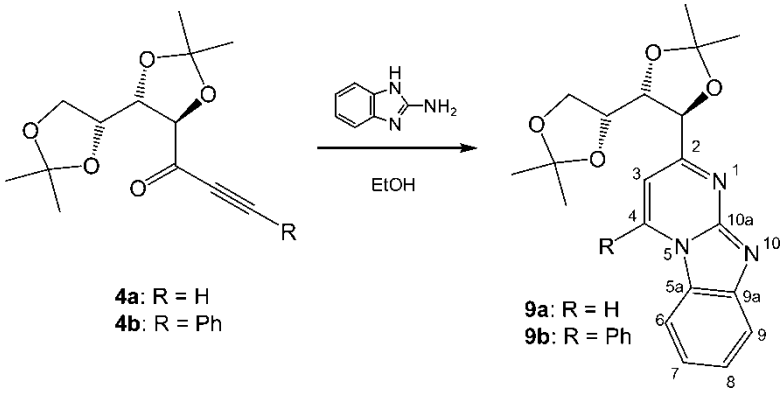
Figure 1: ORTEP drawing of **7f** (only one of the two symmetry independent molecules is shown, the two molecules differ mainly in the position of the phenyl group at C14, dihedral angle N1-C14-C21-C22: – 152.27°, N3-C44-C51-C52: 163.11°).



Scheme 3

scheme of the atoms. The deprotection of compound **7a** by treatment with aqueous trifluoroacetic acid afforded the 4-(D-*xylo*-1,2,3,4-tetrahydroxy-butyl)-2-methyl-pyrimidine **8** in 80% yield (Scheme 3).

On the other hand, ynones **4a**,**b** were reacted with 2-amino-benzimidazol in refluxing ethanol to give the 2-(1,2:3,4-di-*O*-isopropylidene-D-*xylo*-1,2,3,4-tetrahydroxy-butyl)benzo[4,5]imidazo[1,2-*a*]pyrimidines **9a**,**b** in good yields (Scheme 4). The crystallographic data of **9a** were in agreement with the proposed reaction pathway (Figure 2). The comparison with the spectra of the similar 2-(methyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-deoxy-α-D-altropyranosid-3-yl-methyl)benzo [4,5]imidazo[1,2-*a*]pyrimidines,[18] whose structures were analyzed by means of HMBC and NOE experiments, allowed the assignment of all ^{13}C NMR signals. Due to the anisotropy effect of the phenyl ring, the signal of H-6 ($\delta = 6.63$) in the ^{1}H NMR spectrum of **9b** is significantly upfield shifted compared with the H-6 ($\delta = 7.81$) signal in the ^{1}H NMR spectrum of **9a**.



Scheme 4

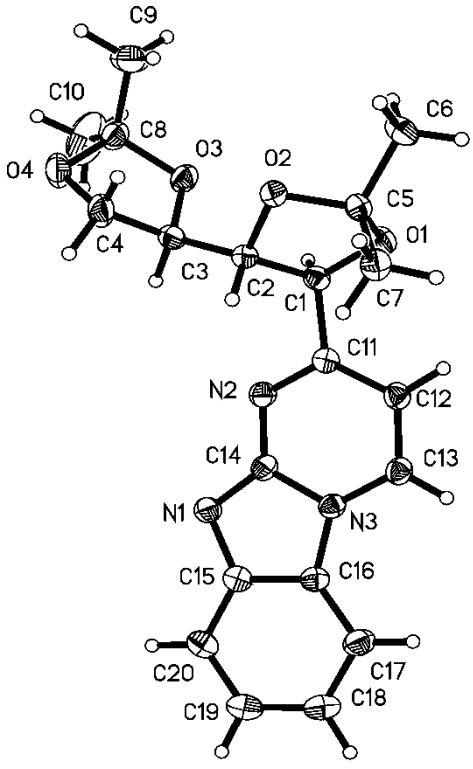
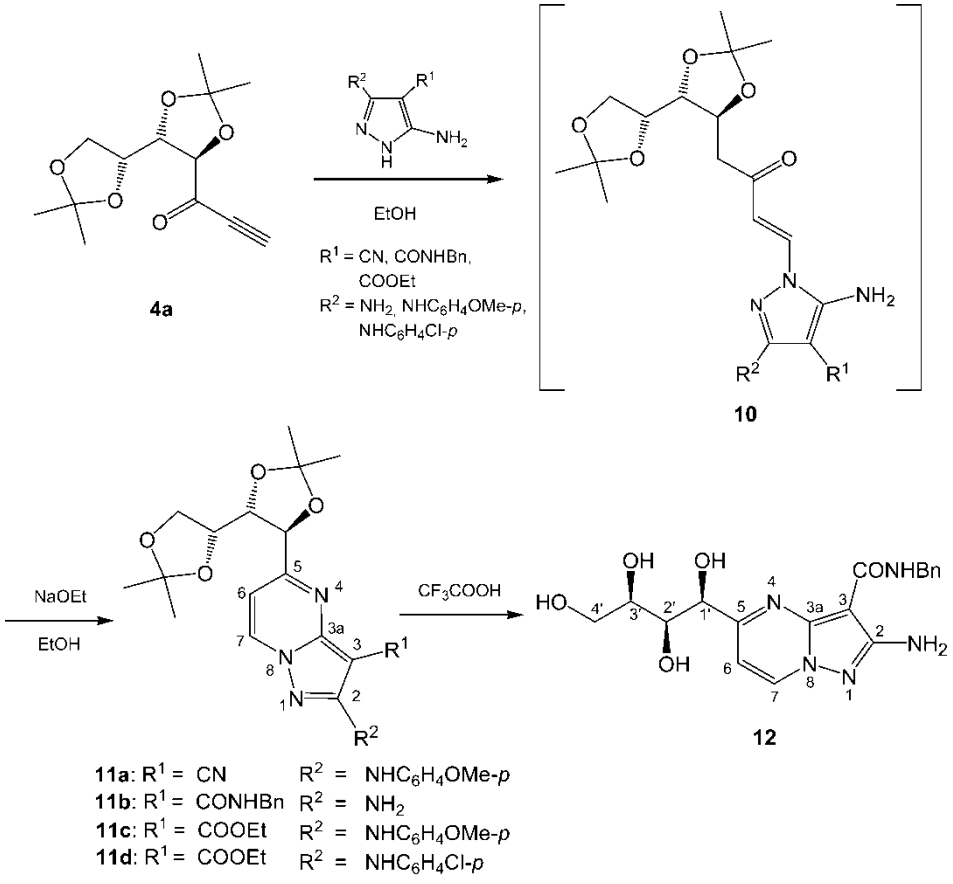


Figure 2: ORTEP drawing of **9a**.

In a similar way the pyrazolo[1,5-*a*]pyrimidines **11a–d** could be obtained by reaction of terminal ynone **4a** with various 5-amino-pyrazole carbonic acid derivatives. A mixture of ynone **4a** and 5-amino-pyrazole carbonic acid derivatives was refluxed in ethanol until the starting material was consumed and the intermediates **10a–d** were formed. The synthesis of the polycyclic compounds **11a–d** as white and yellow crystals, respectively, can then be accomplished in excellent yields after addition of a sodium ethanolate solution to the reaction mixture at room temperature. The structure of the intermediates **10a–d** was verified by NMR studies. The presence of these intermediates confirmed once again the postulated reaction pathways. As expected, for the compounds **11a–d** no signals of the acetylenic carbon atoms were observed in the ^{13}C NMR spectra. The structure was proven by the crystallographic data of **11c** (Scheme 5).

We examined the deprotection of compound **11b**. The cleavage of the isopropylidene groups was performed in a mixture of trifluoroacetic acid and water to afford the 2-amino-*N*-benzyl-5-(D-*xylo*-1,2,3,4-tetrahydroxy-butyl) pyrazolo[1,5-*a*]pyrimidine-3-carboxamide **12**. The polycyclic acyclo-*C*-nucleoside **12** was obtained as a white solid in 72% yield.



Scheme 5

EXPERIMENTAL

Melting points were measured with a Boëtius apparatus and are corrected. Specific rotations were determined with a Polar LμP polarimeter (IBZ Messtechnik). IR spectra were recorded with a Nicolet 205 FT-IR spectrometer. ^{1}H NMR (500.13, 300.13, and 250.13 MHz) and ^{13}C NMR (125.7, 75.5 MHz, and 62.9 MHz) spectra were recorded on Bruker instruments AVANCE 500, ARX 300, and AC 250, respectively, with $CDCl_3$ as solvent unless otherwise stated. The calibration of spectra was carried out on $CDCl_3$ (^{1}H, ^{13}C) signals ($\delta\ ^{1}H_{CDCl_3} = 7.25$; $\delta\ ^{13}C_{CDCl_3} = 77.0$). The ^{13}C NMR signals were assigned by DEPT and/or two-dimensional ^{13}C,^{1}H correlation spectra. The mass spectra were recorded on an AMD 402/3 spectrometer (AMD Intectra GmbH). For chromatography, Merck silica gel 60 (230–400 mesh) was used. TLC was performed on silica gel 60 GF_{254} (Merck) with detection by using UV light

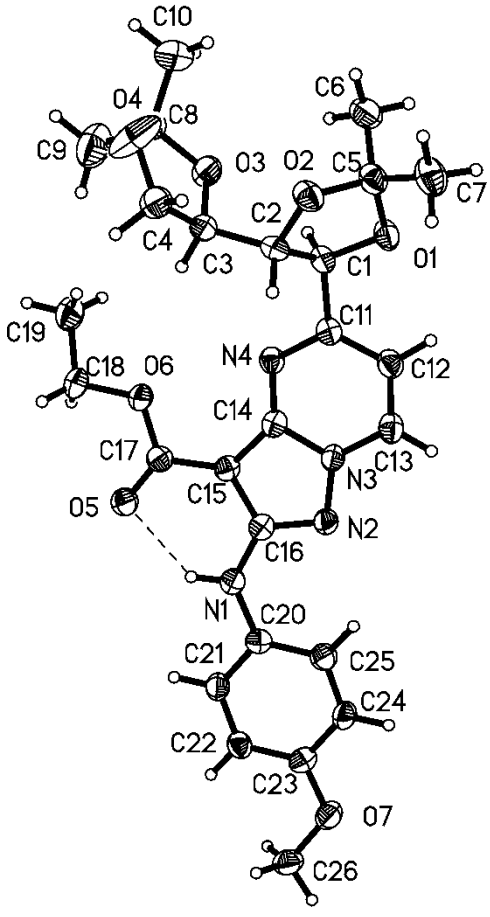


Figure 3: ORTEP drawing of **11c**.

and charring with sulfuric acid. Elemental analysis was performed on a Leco CHNS-932 instrument. Solvents were distilled and, if necessary, dried using standard procedures. The data collections were performed on a Bruker X8Apex CCD diffractometer system with Mo-K_α radiation ($\lambda = 0.71073$ Å) and a graphite monochromator with φ and ω scans after checking the crystal quality by collecting reflections from 60 frames and determining a reasonable reduced cell. The structures were solved by direct methods (Bruker SHELXTL) and refined by the full matrix least-squares method of the Bruker SHELXTL software package. All nonhydrogen atoms were refined anisotropically with the hydrogen atoms introduced into theoretical positions and refined according to the riding model. CCDC 276684, 276685, and 276686 contain the supplementary crystallographic data for compounds **7f**, **9a**, and **11c**, respectively. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.

html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).

1,2-Dideoxy-4,5:6,7-di-*O*-isopropylidene-D-*ido*, *gulo*-hept-1-ynitol (3a)

Ethynylmagnesium bromide (35 mL, 0.5 M solution in THF) was added dropwise to a solution of 2,3:4,5-di-*O*-isopropylidene-D-xylose **2** (2.00 g, 8.7 mmol) in dry THF (50 mL) at 0°C. The mixture was stirred for 4 h at rt, poured into water (20 mL), and extracted with dichloromethane (3 × 20 mL). Then the combined organic phases were washed with water (2 × 20 mL), dried (Na_2SO_4), and evaporated under reduced pressure. The residue was purified by column chromatography (toluene/EtOAc 2 : 1). Compound **3a** was isolated as colorless syrup. Yield: 1.44 g (65%); 2 : 3-mixture of R/S and S/R, respectively; $[\alpha]_D^{24}$ +3.9° (*c* 1.0, $CHCl_3$); R_f 0.38 (toluene/ethyl acetate, 2 : 1). IR (Film), ν (cm^{-1}): 3434 (OH); 3266 (≡CH); 2117 (C≡C). ^1H NMR (250 MHz): δ = 4.53–4.46, 4.45–4.39 (2 × m, 1H, H-3), 4.33–4.23 (m, 1H, H-4), 4.16–4.09 (m, 2H, H-5, H-6), 4.05 (dd, 1H, $^3J_{6,7a}$ = 6.7 Hz, $^2J_{7a,7b}$ = 8.0 Hz, H-7a), 3.92 (t, 1H, $^3J_{6,7b}$ = 8.0 Hz, H-7b), 2.73, 2.67 (2 × d, 1H, $^3J_{3,OH}$ = 7.3, 5.2 Hz, OH), 2.54, 2.52 (2 × d, 1H, $^4J_{1,3}$ = 1.8, 0.6 Hz, H-1), 1.45, 1.44, 1.42, 1.37 (4 × s, 12H, 4 × Me). ^{13}C NMR (125.7 MHz): δ = 110.6, 110.3, 109.8, 109.7 (2 × *C*(Me)$_2$), 81.6, 81.0 (C-1), 79.5, 78.9 (C-4), 77.1, 76.9 (C-5), 75.3, 75.1 (C-2), 74.9, 74.6 (C-6), 65.8, 65.7 (C-7), 62.6, 62.4 (C-3), 27.3, 27.2, 27.1, 26.1, 25.5, 25.4 (4 × Me). MS (EI), *m*/*z* (%): 257 (3) $[MH]^+$.

Anal. Calcd for $C_{13}H_{20}O_5$(256.13): C, 60.92; H, 7.87. Found: C, 60.72; H, 7.81.

1,2-Dideoxy-4,5:6,7-di-*O*-isopropylidene-1-phenyl-D-*ido*, *gulo*-hept-1-ynitol (3b)

The reaction of **2** (2.00 g, 8.7 mmol) with lithium phenylacetylide (17 mL, 1.0 M solution in THF) was carried out as described above for the preparation of **3a**. The product was purified by column chromatography (toluene/EtOAc 4 : 1). Compound **3b** was isolated as colorless syrup. Yield: 1.79 g (62%); 2 : 3-mixture of R/S and S/R, respectively; $[\alpha]_D^{23}$ − 9.3° (*c* 1.0, $CHCl_3$); R_f 0.36 (toluene/ethyl acetate, 4 : 1). IR (Film), ν (cm^{-1}): 3432 (OH); 2231 (C≡C). ^1H NMR (250 MHz): δ = 7.45–7.39 (m, 2H, Ph), 7.33–7.25 (m, 3H, Ph), 4.75, 4.67 (2 × dd, 1H,, $^3J_{2,3}$ = 3.7, 4.5 Hz, $^3J_{3,OH}$ = 5.2, 6.2 Hz, H-3), 4.38–4.26 (m, 1H, H-4), 4.25–4.16 (m, 2H, H-5, H-6), 4.05 (dd, 1H, $^3J_{6,7a}$ = 6.7 Hz, $^2J_{7a,7b}$ = 8.0, H-7a), 3.95 (t, 1H, $^3J_{6,7b}$ = 8.0, H-7b), 2.85, 2.76 (2 × d, 1H, OH), 1.47, 1.46, 1.43, 1.36 (4 × s, 12H, 4 × Me). ^{13}C NMR (75.5 MHz): δ = 131.7, 128.7, 128.3 (*o*-, *m*-, *p*-Ph), 121.9 (*i*-Ph), 110.5, 110.2, 109.7, 109.6 (2 × *C*(Me)$_2$), 86.8, 86.5, 86.4, 85.9 (C-1, C-2), 79.7, 79.3 (C-4), 76.7 (C-5),

75.4, 75.2 (C-6), 65.8, 65.7 (C-7), 63.5, 62.9 (C-3), 27.34, 27.27, 27.13, 26.07, 25.5, 25.4 (4 × Me). MS (EI), m/z (%): 332 (5) $[M]^+$.

Anal. Calcd for $C_{19}H_{24}O_5$(332.16): C, 68.66; H, 7.28. Found: C, 68.41; H, 7.14.

1,2-Dideoxy-4,5:6,7-di-*O*-isopropylidene-D-*xylo*-hept-1-yn-3-ulose (4a)

To a solution of compound **3a** (0.770 g, 3 mmol) in anhyd. dimethylsulfoxide (4 mL) was given acetic acid anhydride (1.5 mL) and the mixture was stirred at 22°C for 24 h. Then chloroform (30 mL) and cold saturated aqueous $NaHCO_3$ solution were added until neutralization. The mixture was extracted with chloroform (3 × 20 mL), the combined organic layers washed with water, and dried with Na_2SO_4, and the solvent evaporated. The residue was purified by column chromatography (toluene/EtOAc 10 : 1). Compound **4a** was isolated as colorless syrup. Yield: 0.365 g (48%); $[\alpha]_D^{21}$ −14.6° (c 1.5, $CHCl_3$); R_f 0.44 (toluene/ethyl acetate, 10 : 1). IR (Film), ν (cm^{-1}): 3248 (CH); 2094 (C≡C); 1684 (CO). ^{1}H NMR (250 MHz): $\delta = 4.38$ (d, 1H, $^3J_{4,5} = 6.8$ Hz, H-4), 4.26 (dt, 1H, H-6), 4.22 (dd, 1H, $^3J_{5,6} = 4.6$ Hz, H-5), 4.06 (dd, 1H, $^3J_{6,7a} = 6.4$ Hz, $^2J_{7a,7b} = 8.5$, H-7a), 3.87 (dd, 1H, $^3J_{6,7b} = 6.4$ Hz, H-7b), 3.48 (s, 1H, H-1), 1.50, 1.43, 1.42, 1.37 (4 × s, 12H, 4 × Me). ^{13}C NMR (75.5 MHz): $\delta = 186.0$ (C-3), 112.3, 110.0 (2 × $C(Me)_2$), 83.6 (C-1), 82.1 (C-4), 79.4 (C-2), 78.1 (C-5), 75.4 (C-6), 65.5 (C-7), 26.8, 26.1, 26.1, 25.4 (4 × Me). MS (EI), m/z (%): 255 (5) $[MH]^+$.

Anal. Calcd for $C_{13}H_{18}O_5$(254.11): C, 61.40; H, 7.14. Found: C, 60.93; H, 6.68.

1,2-Dideoxy-4,5:6,7-di-*O*-isopropylidene-1-phenyl-D-*xylo*-hept-1-yn-3-ulose (4b)

PCC (0.860 g, 4.0 mmol) was added to a solution of **3a** (0.660 g, 2.0 mmol) in dry dichloromethane (40 mL). The mixture was stirred for 12 h, and filtered, and the residue washed with EtOAc. The solvent was removed under reduced pressure and the residue was purified by column chromatography (toluene/EtOAc 10 : 1). Compound **4b** was isolated as a white solid. Yield: 0.340 g (52%); mp 73–75°C; $[\alpha]_D^{22}$ −39.6° (c 1.0, $CHCl_3$); R_f 0.43 (toluene/ethyl acetate, 10 : 1). IR (KBr), ν (cm^{-1}): 2207 (C≡C); 1652 (CO). ^{1}H NMR (250 MHz): $\delta = 7.63$–7.35 (m, 5H, Ph), 4.45 (d, 1H, $^3J_{4,5} = 6.7$ Hz, H-4), 4.35–4.25 (m, 2H, H-5, H-6), 4.09 (dd, 1H, $^3J_{6,7a} = 6.4$ Hz, $^2J_{7a,7b} = 8.5$, H-7a), 3.91 (dd, 1H, $^3J_{6,7b} = 6.4$ Hz, H-7b), 1.53, 1.51, 1.44, 1.39 (4 × s, 12H, 4 × Me). ^{13}C NMR (75.5 MHz): $\delta = 186.3$ (C-3), 133.3, 131.3, 128.7 (o-, m-, p-Ph), 119.5 (i-Ph), 112.2, 110.0 (2 × $C(Me)_2$), 96.2, 86.1 (C-1, C-2), 82.5 (C-4), 78.6 (C-5), 75.8 (C-6), 65.6 (C-7), 26.9, 26.3, 26.2, 25.5 (4 × Me). MS (EI), m/z (%): 330 (5) $[M]^+$.

Anal. Calcd for $C_{19}H_{22}O_5$(330.15): C, 69.07; H, 6.71. Found: C, 68.98; H, 6.66.

3-(1,2:3,4-Di-*O*-isopropylidene-D-*xylo*-1,2,3,4-tetrahydroxy-butyl)-5-phenyl-1*H*(2*H*)pyrazole (5)

A mixture of **4b** (0.165 g, 0.5 mmol) and hydrazine hydrate (0.035 mL, 0.75 mmol) in dry ethanol (5 mL) was stirred for 1 h. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography (toluene/EtOAc 1 : 1). Compound **5** was isolated as colorless syrup. Yield: 0.145 g (85%); $[\alpha]_D^{21}$ −12.6° (*c* 1.0); R_f 0.22 (toluene/ethyl acetate, 2 : 1). ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 8.66–7.58$ (m, 2H, Ph), 7.43–7.30 (m, 3H, Ph), 6.58 (s, 1H, H-4), 5.00 (d, 1H, $^3J_{1',2'} = 8.2$ Hz, H-1′), 4.24 (ddd, 1H, H-3′), 4.15 (dd, 1H, $^3J_{2',3'} = 5.2$ Hz, H-2′), 3.98 (dd, 1H, $^3J_{3',\ 4'a} = 6.7$ Hz, $^2J_{4'a,4'b} = 8.5$ Hz, H-4′a), 3.67 (dd, 1H, $^3J_{3',4'b} = 7.3$, H-4′b), 1.51, 1.50, 1.41, 1.36 (4 × s, 12H, 4 × Me). ^{13}C NMR (75.5 MHz): $\delta = 130.4$ (*i*-Ph), 128.9, 128.4, 125.6 (*o*-, *m*-, *p*-Ph), 110.3, 109.8 (2 × $C(Me)_2$), 100.9 (C-4), 81.5 (C-2′), 75.1 (C-1′), 73.5 (C-3′), 65.5 (C-4′), 26.84, 26.79, 26.2, 25.4 (4 × Me); C-3, C-5 are not given due to strong signal broadening. MS (EI), *m*/*z* (%): 344 (18) $[M]^+$.

Anal. Calcd for $C_{19}H_{24}N_2O_4$(344.17): C, 66.26; H, 7.02; N, 8.13. Found: C, 66.14; H, 7.32; N, 7.60.

3-(D-*xylo*-1,2,3,4-Tetrahydroxy-butyl)- 5-phenyl-1*H*(2*H*)-pyrazole (6)

To a stirred solution of compound **5** (0.220 g, 0.5 mmol) in THF (1 mL) and water (2 mL) was given trifluoroacetic acid (0.075 mL, 1.0 mmol) and the mixture was heated at 65°C until the starting material had disappeared (detected by TLC; approximately 6 h). After filtration through aluminium oxide (90, active basic, Merck), the residue was washed several times with methanol. The combined filtrates were evaporated and the remaining residue was purified by column chromatography (ethyl acetate/methanol, 5 : 1). Compound **6** was isolated as a white foam. Yield: 0.110 g (85%); mp 35–37°C; $[\alpha]_D^{23}$ −0.7° (*c* 0.5, MeOH); R_f 0.33 (ethyl acetate/methanol, 5 : 1). ^{1}H NMR (250 MHz, DMSO-d_6): $\delta = 12.72$ (bs, NH), 7.84–7.68 (m, 2H, Ph); 7.50–7.21 (m, 3H, Ph), 6.56 (s, 1H, H-4), 5.26 (bs, OH-1′), 4.74 (t, 1H, $^3J_{4',OH\text{-}4'} = 5.5$ Hz, OH-4′), 4.64–4.33 (m, 3H, H-1′, OH-2′, OH-3′), 3.63 (m, 1H, H-2′), 3.49–3.26 (m, 3H, H-3′, H-4′). ^{13}C NMR (62.9 MHz, DMSO-d_6): $\delta = 128.9$, 127.6, 125.2 (*o*-, *m*-, *p*-Ph), 100.4 (C-4), 73.6 (C-2′), 71.5 (C-3′), 67.8 (C-1′), 63.1 (C-4′), C-3, C-5, *i*-Ph-C5 are not given due to strong signal broadening. MS (EI), *m*/*z* (%): 264 (4) $[M]^+$.

HRMS Calcd for $C_{13}H_{16}N_2O_4$: 264.11099. Found: 264.11114.

4-(1,2:3,4-Di-*O*-isopropylidene-D-*xylo*-1,2,3,4-tetrahydroxy-butyl)-2-methyl-pyrimidine (7a)

A mixture of **4a** (0.125 g, 0.5 mmol), acetamidinium chloride (0.061 mg, 0.65 mmol), Na_2CO_3 (0.138 g, 1.38 mmol), water (0.01 mL), and EtOAc (5 mL)

was heated under reflux until the starting material had disappeared (1 h, TLC control). Then the solution was filtered and evaporated under reduced pressure. The residue was purified by column chromatography (toluene/ethyl acetate 1 : 1). Compound **7a** was isolated as colorless syrup. Yield: 0.115 g (78%); $[\alpha]_D^{24}$ +23.2° (*c* 1.0, $CHCl_3$); R_f 0.30 (toluene/ethyl acetate 1 : 1). ^{1}H NMR (250 MHz): $\delta = 8.61$ (d, 1H, $^3J_{5,6} = 5.2$ Hz, H-6), 7.33 (d, 1H, H-5), 4.85 (d, 1H, $^3J_{1',2'} = 7.6$ Hz, H-1′), 4.40 (ddd, 1H, H-3′), 4.13 (dd, 1H, $^3J_{3',4'a} = 6.7$ Hz, $^2J_{4'a,4'b} = 8.5$ Hz, H-4′a), 3.99 (dd, 1H, $^3J_{2',3'} = 4.9$ Hz, H-2′), 3.89 (dd, 1H, $^3J_{3',4'b} = 7.0$, H-4′b), 2.68 (s, 3H, 2-Me), 1.54, 1.45, 1.43, 1.41 (4 × s, 12H, 4 × Me). ^{13}C NMR (75.5 MHz): $\delta = 167.9$, 167.7 (C-2, C-4), 157.7 (C-6), 114.3 (C-5), 110.8, 109.8 (2 × *C*(Me)$_2$), 81.8 (C-2′), 78.7 (C-1′), 76.1 (C-3′), 66.1 (C-4′), 26.9, 26.7, 26.3, 25.9, 25.7 (4 × Me, 2-Me). MS (CI), *m*/*z* (%): 295 (100) $[MH]^+$.

Anal. Calcd for $C_{15}H_{22}N_2O_4$(294.16): C, 61.21; H, 7.53; N, 9.52. Found: C, 61.08; H, 7.58; N, 9.03.

4-(1,2:3,4-Di-*O*-isopropylidene-D-*xylo*-1,2,3,4-tetrahydroxybutyl)-2-phenyl-pyrimidine (7b)

The reaction of **4a** (0.125 g, 0.5 mmol) with benzamidinium chloride (0.102 g, 0.65 mmol) was carried out as described above for the preparation of **7a**. The product was purified by column chromatography (toluene/ethyl acetate, 10 : 1). Compound **7b** was isolated as a white solid. Yield: 0.110 g (63%); mp 82–84°C; $[\alpha]_D^{23}$ +18.7° (*c* 1.0, $CHCl_3$); R_f 0.44 (toluene/ethyl acetate, 10 : 1). ^{1}H NMR (250 MHz): $\delta = 8.80$ (d, 1H, $^3J_{5,6} = 4.9$ Hz, H-6), 8.46–8.37 (m, 2H, *o*-Ph), 7.52–7.45 (m, 3H, *m*-, *p*-Ph), 7.44 (d, 1H, H-5), 5.01 (d, 1H, $^3J_{1',2'} = 7.6$ Hz, H-1′), 4.52 (ddd, 1H, H-3′), 4.20 (dd, 1H, $^3J_{3',4'a} = 6.4$ Hz, $^2J_{4'a,4'b} = 8.5$ Hz, H-4 a), 4.13 (dd, 1H, $^3J_{2',3'} = 4.9$ Hz, H-2′), 3.96 (dd, 1H, $^3J_{3',4'b} = 7.3$, H-4′b), 1.58, 1.50, 1.45 (3 × s, 12H, 4 × Me). ^{13}C NMR (75.5 MHz): $\delta = 168.3$ (C-4), 163.9 (C-2), 158.0 (C-6), 137.2 (*i*-Ph), 130.9, 128.6, 128.3, 127.9 (*o*-, *m*-, *p*-Ph), 115.2 (C-5), 110.9, 109.8 (2 × *C*(Me)$_2$), 81.8 (C-2′), 78.8 (C-1′), 76.3 (C-3′), 66.1 (C-4′), 26.9, 26.8, 26.3, 25.8 (4 × Me). MS (FAB^+), *m*/*z* (%): 357 (100) $[MH]^+$.

Anal. Calcd for $C_{20}H_{24}N_2O_4$ (356.17): C, 67.40; H, 6.79; N, 7.86. Found: C, 66.99; H, 6.80; N, 6.97.

4-(1,2:3,4-Di-*O*-isopropylidene-D-*xylo*-1,2,3,4-tetrahydroxybutyl)-2-methylthio-pyrimidine (7c)

The reaction of **4a** (0.125 g, 0.5 mmol) with *S*-methyl-isothiouronium sulfate (0.180 g, 0.65 mmol) was carried out as described above for the preparation of **7a**. The product was purified by column chromatography (toluene/ethyl acetate, 10 : 1). Compound **7c** was isolated as a white solid.

Yield: 0.095 g (58%); mp 66–68°C; $[\alpha]_D^{21}$ +53.5° (*c* 1.0, $CHCl_3$); R_f 0.38 (toluene/ethyl acetate, 10 : 1). ^{1}H NMR (250 MHz): $\delta = 8.48$ (d, 1H, $^3J_{5,6} = 4.9$ Hz, H-6), 7.16 (d, 1H, H-5), 4.84 (d, 1H, $^3J_{1',2'} = 7.6$ Hz, H-1′), 4.38 (ddd, 1H, H-3′), 4.08 (dd, 1H, $^3J_{3',\ 4'a} = 6.4$ Hz, $^2J_{4'a,4'b} = 8.5$ Hz, H-4′a), 4.02 (dd, 1H, $^3J_{2',3'} = 4.6$ Hz, H-2′), 3.89 (dd, 1H, $^3J_{3',4'b} = 7.3$, H-4′b), 2.51 (s, 3H, SMe), 1.51, 1.42, 1.41, 1.38 (4 × s, 12H, 4 × Me). ^{13}C NMR (62.9 MHz): $\delta = 172.3$ (C-2); 168.3 (C-4), 157.8 (C-6), 112.4 (C-5), 110.9, 109.7 (2 × *C*$(Me)_2$); 81.4 (C-2′), 78.4 (C-1′), 75.9 (C-3′), 65.9 (C-4′), 26.8, 26.6, 26.2, 25.6 (4 × Me), 13.9 (SMe). MS (EI), *m*/*z* (%): 326 (2) $[M]^+$.

Anal. Calcd for $C_{15}H_{22}N_2O_4S$ (326.13): C, 55.19; H, 6.79; N, 8.58; S 9.82. Found: C, 55.45; H, 6.81; N, 8.14; S, 9.89.

4-(1,2:3,4-Di-*O*-isopropylidene-D-*xylo*-1,2,3,4-tetrahydroxybutyl)-2-methoxy-pyrimidine (7d)

The reaction of **4a** (0.125 g, 0.5 mmol) with *O*-methyl-isothiouronium sulfate (0.180 g, 0.65 mmol) was carried out as described above for the preparation of **7a**. The product was purified by column chromatography (toluene/ethyl acetate, 3 : 1). Compound **7d** was isolated as a white solid. Yield: 0.100 g (65%); mp 41–43°C; $[\alpha]_D^{23}$ +28.8° (*c* 1.0, $CHCl_3$); R_f 0.28 (toluene/ethyl acetate, 3 : 1). ^{1}H NMR (250 MHz): $\delta = 8.49$ (d, 1H, $^3J_{5,6} = 4.9$ Hz, H-6), 7.16 (d, 1H, H-5), 4.85 (d, 1H, $^3J_{1',2'} = 7.6$ Hz, H-1′), 4.41 (ddd, 1H, H-3′), 4.10 (dd, 1H, $^3J_{3',\ 4'a} = 6.7$ Hz, $^2J_{4'a,4'b} = 8.5$ Hz, H-4′a), 4.05 (dd, 1H, $^3J_{2',3'} = 4.6$ Hz, H-2′), 3.97 (s, 3H, OMe); 3.93 (dd, 1H, $^3J_{3',4'b} = 7.3$, H-4′b), 1.52, 1.44, 1.42, 1.38 (4 × s, 12H, 4 × Me). ^{13}C NMR (62.9 MHz): $\delta = 170.8$, 165.1 (C-2, C-4), 160.0 (C-6), 111.1 (C-5), 110.9, 109.7 (2 × *C*$(Me)_2$), 81.5 (C-2′), 78.4 (C-1′), 75.9 (C-3′), 65.9 (C-4′), 54.9 (OMe), 26.9, 26.7, 26.2, 25.6 (4 × Me). MS (EI), *m*/*z* (%): 310 (2) $[M]^+$.

Anal. Calcd for $C_{15}H_{22}N_2O_5$ (310.35): C, 58.05; H, 7.15; N, 9.03. Found: C, 57.78; H, 7.07; N, 8.54.

4-(1,2:3,4-Di-*O*-isopropylidene-D-*xylo*-1,2,3,4-tetrahydroxybutyl)-2-methyl-6-phenyl-pyrimidine (7e)

The reaction of **4b** (0.165 g, 0.5 mmol) with acetamidinium chloride (0.061 mg, 0.65 mmol) was carried out as described above for the preparation of **7a**. The product was purified by column chromatography (toluene/ethyl acetate, 4 : 1). Compound **7e** was isolated as a white solid. Yield: 0.165 g (90%); mp 70–72°C; $[\alpha]_D^{21}$ −2.1° (*c* 1.0, $CHCl_3$); R_f 0.50 (toluene/ethyl acetate, 4 : 1). ^{1}H NMR (250 MHz): $\delta = 8.12$–8.03 (m, 2H, Ph), 7.73 (s, 1H, H-5), 7.53–7.46 (m, 3H, Ph), 4.92 (d, 1H, $^3J_{1',2'} = 7.6$ Hz, H-1′), 4.46 (ddd, 1H, H-3′), 4.17 (dd, 1H, $^3J_{3',\ 4'a} = 6.7$ Hz, $^2J_{4'a,4'b} = 8.5$ Hz, H-4′a), 4.06 (dd, 1H, $^3J_{2',3'} = 5.2$ Hz, H-2′), 3.95 (dd, 1H, $^3J_{3',4'b} = 7.3$ Hz, H-4′b), 2.75 (s, 3H, 2-Me),

1.58, 1.51, 1.45, 1.43 (4 × s, 12H, 4 × Me). ^{13}C NMR (125.7 MHz): $\delta = 168.4$, 167.9 (C-4, C-6), 164.9 (C-2), 137.2 (*i*-Ph), 130.8, 128.9, 127.3 (*o*-, *m*-, *p*-Ph), 109.9 (C-5), 110.8, 109.7 (2 × *C*(Me)$_2$), 81.9 (C-2′), 78.9 (C-1′), 76.2 (C-3′), 66.2 (C-4′), 26.9, 26.8, 26.3, 26.1, 25.7 (4 × Me, 2-Me). MS (CI), *m*/*z* (%): 371 (100) $[MH]^+$.

Anal. Calcd for $C_{21}H_{26}N_2O_4$ (370.19): C, 68.09; H, 7.07; N, 7.56. Found: C, 67.59; H, 6.71; N, 7.39.

4-(1,2:3,4-Di-*O*-isopropylidene-D-*xylo*-1,2,3,4-tetrahydroxybutyl)-2,6-diphenyl-pyrimidine (7f)

The reaction of **4b** (0.165 g, 0.5 mmol) with benzamidinium chloride (0.102 g, 0.65 mmol) was carried out as described above for the preparation of **7a**. Recrystallization from ethyl acetate gave **7f** as colorless needles. Yield: 0.205 g (96%); mp 135–138°C; $[\alpha]_D^{23}$ +49.2° (*c* 1.0, $CHCl_3$); R_f 0.63 (toluene/ethyl acetate, 10 : 1). ^{1}H NMR (250 MHz): $\delta = 8.62$–8.54 (m, 2H, Ph), 8.30–8.21 (m, 2H, Ph), 7.86 (d, 1H, $^4J_{1',5} = 0.6$ Hz, H-5), 7.60–7.47 (m, 6H, Ph), 5.07 (dd, 1H, $^3J_{1',2'} = 7.6$ Hz, H-1′), 4.58 (ddd, 1H, H-3′), 4.24 (dd, 1H, $^3J_{3',4'a} = 6.4$ Hz, $^2J_{4'a,4'b} = 8.5$ Hz, H-4′a), 4.20 (dd, 1H, $^3J_{2',3'} = 5.2$ Hz, H-2′), 4.02 (dd, 1H, $^3J_{3',4'b} = 7.6$, H-4′b), 1.63, 1.56, 1.47 (3 × s, 12H, 4 × Me). ^{13}C NMR (75.5 MHz): $\delta = 168.8$ (C-4), 164.8, 163.9 (C-2, C-6), 137.5, 137.0 (2 × *i*-Ph), 130.9, 130.8, 128.9, 128.5, 128.1, 127.2 (*o*-, *m*-, *p*-Ph), 110.5 (C-5), 110.9, 109.8 (2 × *C*(Me)$_2$), 81.8 (C-2′), 78.9 (C-1′), 76.4 (C-3′), 66.2 (C-4′), 26.9, 26.8, 26.3, 25.8 (4 × Me). MS (EI), *m*/*z* (%):432 (2) $[M]^+$.

Anal. Calcd for $C_{26}H_{28}N_2O_4$ (432.20): C, 72.20; H, 6.53; N, 6.48. Found: C, 72.16; H, 6.65; N, 6.20.

X-ray Structure Determination of ***7f***

Temperature: 173(2) K; crystal system: triclinic; space group: P1; unit cell dimensions: a = 8.6481(2) Å, b = 10.7316(3) Å, c = 13.3576(3) Å, $\alpha = 71.9460(10)°$, $\beta = 84.3760(10)°$, $\gamma = 74.0510(10)°$; volume: 1133.17(5) Å^3; Z: 2; density (calculated): 1.268 Mg/m^3; absorption coefficient: 0.086 mm^{-1}; F(000): 460; crystal size: 0.63 × 0.29 × 0.20 mm^3; Θ range for data collection: 2.95 to 27.50°; index ranges: $-11 \le h \le 11$, $-13 \le k \le 13$, $-17 \le l \le 17$; reflections collected: 48773; independent reflections: 10038 [R(int) = 0.0318]; completeness to Θ = 27.50°: 97.7%; absorption correction: multiscan (min; max transitions: 0.9480; 0.9831); data/restraints/parameters: 10038/3/577; goodness-of-fit on F^2: 1.030: final R indices [$I > 2\sigma(I)$]: R1 = 0.0372, wR2 = 0.0979; R indices (all data): R1 = 0.0466, wR2 = 0.1072; absolute structure parameter: −0.1(5); largest diff. peak and hole: 0.247 and −0.188 e.Å^{-3}. The weighting scheme was calculated according to $w^{-1} = \sigma^2 (F_o^2) + (0.0633\ P)^2 + 0.1228\ P$ with $P = (F_o^2 + 2\ F_c^2)/3$.

4-(D-*xylo*-1,2,3,4-Tetrahydroxy-butyl)-2-methyl-pyrimidine (8)

The deprotection of compound **7a** (0.145 g, 0.5 mmol) was carried out as described above for the preparation of **6** (reaction time 2 h). The product was purified by column chromatography (ethyl acetate/methanol, 5 : 1). Compound **8** was isolated as a colorless syrup. Yield: 0.086 g (80%); $[\alpha]_D^{23}$ +60.7° (*c* 1.0, MeOH); R_f 0.21 (ethyl acetate/methanol, 5 : 1). ^{1}H NMR (500 MHz, DMSO-d_6): $\delta = 8.62$ (d, 1H, $^3J_{5,6} = 5.1$ Hz, H-6), 7.38 (d, 1H, H-5), 5.45 (d, 1H, $^3J_{1',OH\text{-}1'} = 5.4$ Hz, OH-1′), 4.64 (d, 1H, $^3J_{3',OH\text{-}3'} = 4.7$ Hz, OH-3′), 4.63 (dd, 1H, $^3J_{1',2'} = 3.1$ Hz, H-1′), 4.59 (t, 1H, $^3J_{4',OH\text{-}4'} = 5.5$ Hz, OH-4′), 4.39 (d, 1H, $^3J_{2',OH\text{-}2'} = 7.0$ Hz, OH-2′), 3.81 (ddd, 1H, $^3J_{2',3'} = 4.5$ Hz, H-2′), 3.58 (m, 1H, H-3′), 3.51 (m, 1H, $^3J_{4'a,4'b} = 10.9$ Hz, H-4′a), 3.44 (m, 1H, H-4′b), 2.58 (s, 3H, 2-Me). ^{13}C NMR (62.9 MHz, DMSO-d_6): $\delta = 172.1$ (C-4), 166.3 (C-2), 157.1 (C-6), 116.1 (C-5), 74.0 (C-1′), 73.2 (C-3′), 73.1 (C-2′), 62.6 (C-4′), 25.8 (2-Me). MS (FAB$^+$), *m/z* (%):215 (50) $[MH]^+$.

HRMS Calcd for $C_9H_{14}N_2O_4Na$: 237.08458. Found: 237.08525.

2-(1,2:3,4-Di-*O*-isopropylidene-D-*xylo*-1,2,3,4-tetrahydroxy-butyl)benzo(4,5)imidazo(1,2-*a*)pyrimidine (9a)

A mixture of **4a** (0.125 g, 0.5 mmol) and 2-amino-benzimidazol (0.073 g, 0.55 mmol) in ethanol (5 mL) was heated under reflux for 4 h. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography (toluene/ethyl acetate, 1 : 1). Recrystallization from ethyl acetate gave **9a** as yellow plates. Yield: 0.145 g (78%); mp 168–171°C; $[\alpha]_D^{22}$ +52.5° (*c* 1.0, $CHCl_3$); R_f 0.37 (toluene/ethyl acetate, 1 : 1). ^{1}H NMR (250 MHz): $\delta = 8.74$ (d, 1H, $^3J_{3,4} = 7.0$ Hz, H-4), 7.96 (dt, 1H, $^5J_{6,9} = {}^4J_{7,9} = 1.0$ Hz, $^3J_{8,9} = 8.0$ Hz, H-9), 7.86 (dt, 1H, $^4J_{6,8} = 1.0$ Hz, $^3J_{6,7} = 8.0$ Hz, H-6), 7.55 (dt, 1H, $^3J_{7,8} = 8.0$ Hz, H-8), 7.40 (dt, 1H, H-7), 7.23 (d, 1H, H-3), 5.09 (d, 1H, $^3J_{1',2'} = 7.6$ Hz, H-1′), 4.56 (ddd, 1H, H-3′), 4.26 (dd, 1H, $^3J_{2',3'} = 4.3$ Hz, H-2′), 4.15 (dd, 1H, $^3J_{3',\ 4'a} = 6.7$ Hz, $^2J_{4'a,4'b} = 8.5$ Hz, H-4′a), 3.96 (dd, 1H, $^3J_{3',4'b} = 7.3$, H-4′b), 1.58, 1.48, 1.45, 1.40 (4 × s, 12H, 4 × Me). ^{13}C NMR (75.5 MHz): $\delta = 166.5$ (C-2), 149.8 (C-10a), 144.4 (C-9a), 133.5 (C-4), 126.7 (C-5a), 126.6 (C-8), 122.1 (C-7), 120.5 (C-9), 110.5 (C-6), 111.0, 109.7 (2 × *C*(Me)$_2$), 104.0 (C-3), 81.1 (C-2′), 78.9 (C-1′), 75.7 (C-3′), 66.0 (C-4′), 26.8, 26.7, 26.2, 25.7 (4 × Me). MS (EI), *m/z* (%): 369 (15) $[M]^+$.

Anal. Calcd for $C_{20}H_{23}N_3O_4$ (369.17): C, 65.03; H, 6.28; N, 11.37. Found: C, 64.64; H, 6.33; N, 11.15.

X-ray Structure Determination of ***9a***

temperature: 173(2) K; crystal system: monoclinic; space group: $P2_1$; unit cell dimensions: a = 5.32380(10) Å, b = 10.6952(2) Å, c = 16.1617(3) Å,

$\alpha = 90^\circ$, $\beta = 93.8530(10)^\circ$, $\gamma = 90^\circ$; volume: 918.15(3) Å^3; Z: 2; density (calculated): 1.336 Mg/m^3; absorption coefficient: 0.094 mm^{-1}; F(000): 392; crystal size: 0.58 × 0.48 × 0.18 mm^3; Θ range for data collection: 3.16 to 29.99°; index ranges: $-7 \le h \le 7$, $-14 \le k \le 14$, $-22 \le l \le 22$; reflections collected: 28155; independent reflections: 5324 [R (int) = 0.0235]; completeness to Θ = 29.99°: 99.8%; absorption correction: multiscan (min, max transitions: 0.9473; 0.9832); data/restraints/parameters: 5324/1/248; goodness-of-fit on F^2: 1.033: final R indices [$I > 2\sigma(I)$]: R1 = 0.0330, wR2 = 0.0866; R indices (all data): R1 = 0.0349, wR2 = 0.0885; absolute structure parameter: −0.1(5); largest diff. peak and hole: 0.280 and −0.225 e.Å^{-3}; the weighting scheme was calculated according to $w^{-1} = \sigma^2 (F_o^2) + (0.0573\ P)^2 + 0.1080\ P$ with $P = (F_o^2 + 2\ F_c^2)/3$.

2-(1,2:3,4-Di-*O*-isopropylidene-D-xylo-1,2,3,4-tetrahydroxy-butyl)-4-phenyl-benzo(4,5)imidazo(1,2-*a*)pyrimidine (9b)

The reaction of **4b** (0.165 g, 0.5 mmol) with 2-amino-benzimidazol (0.073 g, 0.55 mmol) was carried out as described above for the preparation of **9a**. The product was purified by column chromatography (toluene/ethyl acetate 1 : 1). Recrystallization from ethyl acetate gave **9b** as yellow needles. Yield: 0.145 g (65%); mp 158–160°C; $[\alpha]_D^{23}$ −3.7° (*c* 1.0, $CHCl_3$); R_f 0.39 (toluene/ethyl acetate, 1 : 1). ^{1}H NMR (250 MHz): δ = 7.95 (dt, 1H, $^5J_{6,9}$, $^4J_{7,9}$ = 1.0 Hz, $^3J_{8,9}$ = 8.0 Hz, H-9), 7.73–7.55 (m, 5H, Ph), 7.45 (dt, 1H, $^3J_{7,8}$ = 8.0 Hz, $^4J_{6,8}$ = 1.0 Hz, H-8), 7.07 (s, 1H, H-3), 7.04 (dt, 1H, $^3J_{6,7}$ = 8.0 Hz, H-7), 6.69 (dt, 1H, H-6), 5.14 (d, 1H, $^3J_{1',2'}$ = 7.6 Hz, H-1′), 4.61 (ddd, 1H, H-3′), 4.32 (dd, 1H, $^3J_{2',3'}$ = 4.6 Hz, H-2′), 4.20 (dd, 1H, $^3J_{3',\ 4'a}$ = 6.4 Hz, $^2J_{4'a,4'b}$ = 8.2 Hz, H-4′a), 4.01 (dd, 1H, $^3J_{3',4'b}$ = 7.3, H-4′b), 1.57, 1.49, 1.46, 1.43 (4 × s, 12H, 4 × Me). ^{13}C NMR (75.5 MHz): δ = 165.7 (C-2), 151.1, 150.0 (C-4, C-10a), 145.0 (C-9a), 132.2 (*i*-Ph), 131.2, 129.4, 128.2, 126.2 (*m*-, *o*-, *p*-Ph), 127.3 (C-5a), 126.6 (C-8), 121.4, 120.4 (C-7, C-9), 114.7 (C-6); 110.9, 109.7 (2 × *C*(Me)$_2$), 105.2 (C-3), 81.1 (C-2′), 79.0 (C-1′), 75.8 (C-3′), 66.1 (C-4′), 26.8, 26.8, 26.3, 25.7 (4 × Me). MS (EI), *m*/*z* (%): 445 (21) [M]$^+$.

Anal. Calcd for $C_{26}H_{27}N_3O_4$ (445.20): C, 70.09; H, 6.11; N, 9.43. Found: C, 70.44; H, 6.15; N, 9.05.

2-(p-Anisidino)-5-(1,2:3,4-di-*O*-isopropylidene-D-*xylo*-1,2,3,4-tetrahydroxy-butyl)pyrazolo(1,5-*a*)pyrimidine-3-carbonitrile (11a)

A mixture of **4a** (0.125 g, 0.5 mmol) and 5-amino-3-(*p*-anisidino)-1*H*-pyrazole-4-carbonitrile (0.115 g, 0.5 mmol) in ethanol (5 mL) was heated under reflux for 4 h, cooled to 20°C, treated with sodium ethanolate

(1.5 mmol) in ethanol (5 mL), and stirred for 1 h. After neutralization with amberlite IR-120 (Fluka-Chemie GmbH), the solvent was removed under reduced pressure and the residue was purified by column chromatography (toluene/ethyl acetate, 2 : 1). Compound **11a** was isolated as a yellow solid. Yield: 0.170 g (75%); mp 131–133°C; $[\alpha]_D^{25}$ +18.8° (*c* 0.5, $CHCl_3$); R_f 0.50 (toluene/ethyl acetate, 2 : 1). IR (KBr), ν (cm^{-1}): 3316 (NH); 2218 (CN). ^1H NMR (500 MHz, DMSO-d_6): $\delta = 9.35$ (s, 1H, NH), 9.06 (d, 1H, $^3J_{6,7} = 6.9$ Hz, H-7), 7.61–7.57 (m, 2H, H_o-NHC_6H_4), 7.19 (d, 1H, H-6), 6.92–6.88 (m, 2H, H_m-NHC_6H_4), 4.95 (d, 1H, $^3J_{1',2'} = 7.9$ Hz, H-1′), 4.31 (dt, 1H, H-3′), 4.13 (dd, 1H, $^3J_{2',3'} = 4.5$ Hz, H-2′), 4.07 (dd, 1H, $^3J_{3',\ 4'a} = 6.8$ Hz, $^2J_{4'a,4'b} = 8.4$ Hz, H-4a′), 3.76 (dd, 1H, $^3J_{3',4'b} = 6.8$, H-4′b), 3.73 (s, 3H, OMe), 1.47, 1.46, 1.35, 1.33 (4 × s, 12H, 4 × Me). ^{13}C NMR (75.5 MHz, DMSO-d_6): $\delta = 162.4$ (C-5), 157.7 (C-2), 154.7 (C_p-NHC_6H_4); 150.1 (C-3a), 137.3 (C-7), 133.8 (C_i-NHC_6H_4), 120.6 (C_o-NHC_6H_4), 114.1 (C_m-NHC_6H_4), 113.7 (CN), 110.5, 109.0 (2 × $C(Me)_2$), 106.8 (C-6), 81.1 (C-2′), 78.7 (C-1′), 75.0 (C-3′), 67.1 (C-3), 65.4 (C-4′), 55.4 (OMe), 26.9, 26.8, 26.3, 25.8 (4 × Me). MS (EI), *m*/*z* (%): 465 (100) $[M]^+$.

Anal. Calcd for $C_{24}H_{27}N_5O_5$ (465.20): C, 61.92; H, 5.85; N, 15.04. Found: C, 61.84; H, 5.89; N, 14.80.

2-Amino-*N*-benzyl-5-(1,2:3,4-di-*O*-isopropylidene-D-*xylo*-1,2,3,4-tetrahydroxy-butyl)pyrazolo(1,5-*a*)pyrimidine-3-carboxamide (11b)

The reaction of **4a** (0.125 g, 0.5 mmol) with 3,5-diamino-*N*-benzyl-1*H*-pyrazole-4-carboxamide (115 mg, 0.5 mmol) was carried out as described above for the preparation of **11a**. The product was purified by column chromatography (toluene/ethyl acetate 1 : 1). Compound **11b** was isolated as a yellow solid. Yield: 0.160 g (68%); mp 58–60°C; $[\alpha]_D^{21}$ +42.4° (*c* 1.0, $CHCl_3$); R_f 0.37 (toluene/ethyl acetate, 1 : 1). IR (KBr), ν (cm^{-1}): 3429, 3343, 3321 (NH), 1655 (CO). ^1H NMR (500 MHz): $\delta = 8.42$ (d, 1H, $^3J_{6,7} = 7.0$ Hz, H-7), 7.94 (t, 1H, NH), 7.39–7.31 (m, 4H, Ph), 7.28–7.23 (m, 1H, Ph), 7.02 (d, 1H, H-6), 4.95 (d, 1H, $^3J_{1',2'} = 7.5$ Hz, H-1′), 4.75 (dd, 1H, $^3J_{NH,CH_2} = 6.5$ Hz, $^2J_{CH_2} = 15.0$ Hz, NCH_2), 4.59 (dd, 1H, $^3J_{NH,CH_2} = 5.8$ Hz, NCH_2), 4.21 (dt, 1H, H-3′), 4.08 (dd, 1H, $^3J_{2',3'} = 4.1$ Hz, H-2′), 3.81 (d, 2H, $^3J_{3',4'} = 6.6$ Hz, H-4′), 1.52, 1.41, 1.37, 1.29 (4 × s, 12H, 4 × Me).^{13}C NMR (75.5 MHz): $\delta = 164.1$ (*C*ONH), 161.8 (C-5), 160.6 (C-2), 146.3 (C-3a), 139.1 (*i*-Ph), 134.7 (C-7), 128.6, 127.4, 127.2 (*o*-, *m*-, *p*-Ph), 110.9, 109.8 (2 × $C(Me)_2$), 104.4 (C-6), 87.7 (C-3), 81.2 (C-2′), 78.5 (C-1′), 75.2 (C-3′), 65.5 (C-4′), 42.5 (CH_2Ph), 26.8, 26.6, 26.2, 25.4 (4 × Me). MS (EI), *m*/*z* (%): 467 (50) $[M]^+$.

Anal. Calcd for $C_{24}H_{29}N_5O_5$ (467.22): C, 61.66; H, 6.25; N, 14.98. Found: C, 61.20; H, 6.01; N, 14.37.

Ethyl 2-(*p*-Anisidino)-5-(1,2:3,4-di-*O*-isopropylidene-D-*xylo*-1,2,3,4-tetrahydroxy-butyl)pyrazolo(1,5-*a*)pyrimidine-3-carboxylate (11c)

The reaction of **4a** (0.125 g, 0.5 mmol) with ethyl 5-amino-3-(*p*-anisidino)-1*H*-pyrazole-4-carboxylate (140 mg, 0.5 mmol) was carried out as described above for the preparation of **11a**. The product was purified by column chromatography (toluene/ethyl acetate 4 : 1). Recrystallization from ethyl acetate gave **11c** as yellow needles. Yield: 0.205 g (80%); mp 138–140°C; $[\alpha]_D^{22}$ +29.2° (*c* 0.5, $CHCl_3$); R_f 0.46 (toluene/ethyl acetate, 4 : 1). IR (KBr), ν (cm^{-1}): 3327 (NH); 1668 (CO). ^1H NMR (250 MHz): $\delta = 8.81$ (s, 1H, NH), 8.52 (d, 1H, $^3J_{6,7} = 7.0$ Hz, H-7), 7.61–7.54 (m, 2H, H_o-NHC_6H_4), 7.14 (d, 1H, H-6), 6.94–6.87 (m, 2H, H_m-NHC_6H_4), 4.99 (d, 1H, $^3J_{1',2'} = 7.6$ Hz, H-1′), 4.58–4.48 (m, 1H, H-3′), 4.50–4.31 (m, 2H, OCH_2CH_3), 4.23 (dd, 1H, $^3J_{3',4'a} = 6.5$ Hz, $^2J_{4'a,4'b} = 8.8$ Hz, H-4′a), 4.14 (dd, 1H, $^3J_{2',3'} = 5.5$ Hz, H-2′), 4.10 (dd, 1H, $^3J_{3',4'b} = 7.6$, H-4′b), 3.79 (s, 3H, OMe), 1.58, 1.49, 1.44, 1.43 (4 × s, 12H, 4 × Me), 1.45 (t, 3H, $^3J = 7.1$ Hz, OCH_2CH_3). ^{13}C NMR (125.7 MHz): $\delta = 165.3$ (*C*OOEt), 162.5 (C-5), 159.1 (C-2), 154.9 (C_p-NHC_6H_4), 147.0 (C-3a), 135.1 (C-7), 133.4 (C_i-NHC_6H_4), 120.0 (C_o-NHC_6H_4), 114.4 (C_m-NHC_6H_4), 110.9, 109.7 (2 × *C*(Me)$_2$), 104.9 (C-6), 86.1 (C-3), 81.9 (C-2′), 78.9 (C-1′), 76.6 (C-3′), 66.2 (C-4′), 60.2 (OCH_2CH_3), 55.6 (OMe), 26.9, 26.7, 26.3, 25.9 (4 × Me), 14.6 (OCH_2CH_3). MS (EI), *m*/*z* (%): 512 (100) $[M]^+$.

Anal. Calcd for $C_{26}H_{32}N_4O_7$ (512.23): C, 60.93; H, 6.29; N, 10.93. Found: C, 60.58; H, 6.28; N, 10.66.

X-ray Structure Determination of ***11c***

Temperature: 173(2) K; crystal system: orthorhombic; space group: $P2_12_12_1$; unit cell dimensions: a = 6.8413(5) Å, b = 14.3667(9) Å, c = 25.8351(15) Å, $\alpha = 90°$, $\beta = 90°$, $\gamma = 90°$; volume: 2539.3(3) $Å^3$; Z: 4; density (calculated): 1.341 Mg/m^3; absorption coefficient: 0.098 mm^{-1}; F(000): 1088; crystal size: 0.77 × 0.14 × 0.13 mm^3; Θ range for data collection: 2.94 to 24.00°; index ranges: $-7 \le h \le 7$, $-16 \le k \le 16$, $-27 \le l \le 29$; reflections collected: 17058; independent reflections: 3966 [R(int) = 0.0437]; completeness to Θ = 24.00°: 99.1%; absorption correction: multiscan (min, max transitions: 0.9281; 0.9873); data/restraints/parameters: 3966/0/344; goodness-of-fit on F^2: 1.045: final R indices [$I > 2\sigma(I)$]: R1 = 0.0423, wR2 = 0.1006; R indices (all data): R1 = 0.0556, wR2 = 0.1079; absolute structure parameter: −0.7(13); largest diff. peak and hole: 0.399 and −0.361 e.$Å^{-3}$; the weighting scheme was calculated according to $w^{-1} = \sigma^2 (F_o^2) + (0.0597\ P)^2 + 0.5989P$ with $P = (F_o^2 + 2\ F_c^2)/3$.

Ethyl 2-(*p*-Chloroanilino)-5-(1,2:3,4-di-*O*-isopropylidene-D-*xylo*-1,2,3,4-tetrahydroxy-butyl)pyrazolo(1,5-*a*)pyrimidine-3-carboxylate (11d)

The reaction of **4a** (0.125 g, 0.5 mmol) with ethyl 5-amino-3-(*p*-chloroanilino)-1*H*-pyrazole-4-carboxylate (140 mg, 0.5 mmol) was carried out as described above for the preparation of **11a**. The product was purified by column chromatography (toluene/ethyl acetate 4 : 1). Recrystallization from ethyl acetate gave **11d** as colorless needles. Yield: 0.135 g (53%); mp 158 − 160°C; $[\alpha]_D^{22}$ +41.8° (*c* 1.0, $CHCl_3$); R_f 0.54 (toluene/ethyl acetate, 4 : 1). IR (KBr), ν (cm^{-1}): 3438 (NH), 1664 (CO). ^1H NMR (250 MHz): $\delta = 9.05$ (s, 1H, NH), 8.53 (d, 1H, $^3J_{6,7} = 6.9$ Hz, H-7), 7.64–7.57 (m, 2H, H_o-NHC_6H_4), 7.31–7.22 (m, 2H, H_m-NHC_6H_4), 7.18 (d, 1H, H-6), 5.00 (d, 1H, $^3J_{1',2'} = 7.6$ Hz, H-1′), 4.58–4.46 (m, 1H, H-3′), 4.46–4.32 (m, 2H, OCH_2CH_3), 4.22 (dd, 1H, $^3J_{3',4'a} = 6.5$ Hz, $^2J_{4'a,4'b} = 8.7$ Hz, H-4′a), 4.14 (dd, 1H, $^3J_{2',3'} = 5.4$ Hz, H-2′), 4.10 (dd, 1H, $^3J_{3',4'b} = 7.6$, H-4′b), 1.58, 1.49, 1.45, 1.43 (4 × s, 12H, 4 × Me), 1.45 (t, 3H, $^3J = 7.1$ Hz, OCH_2CH_3). ^{13}C NMR (75.5 MHz): $\delta = 165.3$ (*C*OOEt), 162.9 (C-5); 158.3 (C-2), 146.6 (C-3a), 138.5 (C_i-NHC_6H_4), 135.2 (C-7), 128.9 (C_m-NHC_6H_4), 126.5 (C_p-NHC_6H_4), 119.2 (C_o-NHC_6H_4), 110.9, 109.7 (2 × *C*(Me)$_2$), 105.2 (C-6), 86.4 (C-3), 81.8 (C-2′), 78.8 (C-1′), 76.6 (C-3′), 66.2 (C-4′), 60.3 (OCH_2CH_3), 26.9, 26.6, 26.3, 25.8 (4 × Me), 14.5 (OCH_2CH_3). MS (EI), *m*/*z* (%): 516 (95) $[M]^+$.

Anal. Calcd for $C_{25}H_{29}ClN_4O_6$ (516.18): C, 58.08; H, 5.65; N, 10.84. Found: C, 58.22; H, 5.66; N, 10.71.

2-Amino-*N*-benzyl-5-(D-*xylo*-1,2,3,4-tetrahydroxy-butyl)-pyrazolo(1,5-*a*)pyrimidine-3-carboxamide (12)

The deprotection of compound **11b** (0.115 g, 0.25 mmol) was carried out as described above for the preparation of **6** (reaction time 6 h). The product was purified by column chromatography (ethyl acetate/methanol, 5 : 1). Compound **12** was isolated as a white solid. Yield: 0.070 g (72%); mp 158–160°C; $[\alpha]_D^{21}$ +57.0° (*c* 0.5, MeOH); R_f 0.21 (ethyl acetate/methanol, 5 : 1). ^1H NMR (250 MHz, DMSO-d_6): $\delta = 8.82$ (d, 1H, $^3J_{6,7} = 6.8$ Hz, H-7); 8.32 (t, 1H, NH), 7.44–7.16 (m, 5H, Ph), 7.03 (d, 1H, H-6), 6.44 (s, 2H, NH_2), 5.67 (1H, $^3J_{1',OH\text{-}1'} = 6.2$ Hz, OH-1′), 4.71 (t, 1H, $^3J_{4',OH\text{-}4'} = 5.3$ Hz, OH-4′), 4.66–4.44 (m, 5H, H-1′, OH-2′, OH-3′, CH_2Ph), 3.78 (m, 1H, H-2′), 3.59–3.38 (m, 3H, H-3′, H-4′). ^{13}C NMR (62.9 MHz, DMSO-d_6): $\delta = 164.5$ (*C*ONH), 163.9 (C-5), 161.5 (C-2), 145.9 (C-3a), 140.1 (*i*-Ph), 134.9 (C-7), 128.6, 127.2, 126.8 (*o*-, *m*-, *p*-Ph), 106.3 (C-6), 86.1 (C-3), 74.4 (C-1′), 73.6 (C-3′), 72.5 (C-2′), 62.7 (C-4′), 41.8 (CH_2Ph). MS (ESI): 388 $[MH]^+$.

HRMS Calcd for $C_{18}H_{21}N_5O_5Na$: 410.14349, Found: 410.14363.

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