The development of strategies for obtaining acyclo-C-nucleoside analogues has become an area of growing attention in organic chemistry. These compounds contain nitrogen heterocycles C–C-linked to a polyhydroxyalkyl ether and show important biological activities.

Recently, we have reported the syntheses of a new series of protected acyclic-C-nucleoside analogues obtained by means of a Vilsmeier–Haack reaction of O-benzyl protected glycals. These hexenopyranoside rings with push-pull activation of protected acyclic-C-nucleoside analogues have now described here the ring transformations of 2-formylglycals with 2-cyano-N-(4-methoxyphenyl)acetamide, 2-benzimidazolylacetanitriile, 2-nitromethylbenzimidazole yielding 5-(1,2,4-tri-O-benzyl-D-"arabino/lyxo"-1,2,3,4-tetrahydroxybutyl)-1,2-dihydro-1-(4-methoxyphenyl)-2-oxopyridine-3-carbonitriles (2). 2-(1,2,4-tri-O-benzyl-D-"arabino/lyxo"-1,2,3,4-tetrahydroxybutyl)-4-nitrobenzo[4,5]imidazo[1,2-a]pyridine-4-carbonitriles (3) and 2-(1,2,4-tri-O-benzyl-D-"lyxo"-1,2,3,4-tetrahydroxybutyl)-4-nitrobenzo[4,5]imidazo[1,2-a]pyridine (4), respectively.

The IR spectra of these compounds showed the expected cyano and carbonyl bands and in the $^1$C NMR spectra the absence of signals for the formyl groups was observed. Furthermore, the successful ring transformation was indicated by the typical long range coupling of pyridone protons H-4 and H-6 ($J = 2.7$ Hz) in the $^1$H NMR spectrum due to the W-arrangement of these protons and the appearance of a new signal for the OH group.

On the other hand, the push-pull functionality of 1a, 1b also allowed reactions with C,N-dinucleophiles furnishing polycyclic analogues. When the reactions were carried out under the same conditions but using 2-benzimidazolylacetanitriile and 2-nitromethylbenzimidazole as C,N-dinucleophiles in order to obtain not only polyhydroxyalkylated monocyclic pyridines but also the corresponding polycyclic compounds.

The treatment of 2-formylglycals with 2-cyano-N-(4-methoxyphenyl)acetamide under Knoevenagel–Cope conditions using piperidinium acetate as the most effective catalyst did not afford the branched-chain sugars but yielded in a ring transformation process the dihydro-pyridinecarbonitriles 2a, 2b (Scheme 1).

**Reagents and conditions:** a) piperidine, HOAc, toluene, reflux, 3 h.
Besides the expected condensation reaction at the formyl group an addition of methanol at the double bond had occurred. The structure of 5 was determined by IR, NMR, and mass spectra. The $^1$H,$^1$H coupling constants (Table 1) allowed the assignment of the configuration at C-1' and C-2' (3, R). The values for the $^1$C,$^1$H couplings between H-3 and CN and C-2", respectively, (14 Hz and 6.4 Hz) determined in a coupled $^1$C NMR spectrum confirmed the (E)-configuration of the structure.\(^1\)\(^7\) Compound 3b was also isolated under this conditions but only in a 5% yield.

The catalytic hydrogenation of the compounds was not successful because of the presence of the nitrile and nitro group, respectively. However, the removal of the benzyl groups using iodotrimethylsilane\(^1\)\(^8\),\(^1\)\(^9\) could be achieved. For 2a we examined the deprotection, which afforded the 1,2-dihydro-5-((D-arabino)-1,2,3,4-tetrahydroxybutyl)-1-(4-methoxyphenyl)-2-oxopyridine-3-carbonitrile \((6)\) (Scheme 4).

In conclusion, in this paper we have described a synthesis of special acyclo-C-nucleoside analogues with high functionality and potential biological activity.

Melting points were measured with a Boëtius apparatus and were corrected. Specific rotations were determined with a Polar LuP polarimeter (IBZ Messtechnik). IR spectra were recorded with a Nicolet 205 FT-IR spectrometer. $^1$H NMR (300.13 and 250.13 MHz, respectively) and $^1$C NMR (75.5 MHz and 62.9 MHz) spectra were recorded on Bruker instruments ARX 300 and AC 250, respectively, in CDCl$_3$ (acetone-$d_6$) as solvent. The calibration of spectra was carried out on TMS (internal $^1$H) and CDC$_3$ ($^1$C) signals $\delta$ $^1$H (TMS) = 0; $\delta$ $^1$C (CDCl$_3$) = 77.0). Spectra of 6 in acetone-$d_6$ were calibrated on solvent signals ($\delta$ $^1$H (TMS) = 2.04; $\delta$ $^1$C (CDCl$_3$) = 29.8). The $^1$C NMR signals were assigned by DEPT and/or $^1$H,$^1$C correlation spectra. The mass spectra were recorded on an AMD 4023 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 and charring with sulfuric acid. Elemental analyses were performed on a Leco CHNS-932 instrument.

5-(1,2,4-Tri-O-benzyl-D-arabin-1,2,3,4-tetrahydroxybutyl)-1,2-dihydro-1-(4-methoxyphenyl)-2-oxopyridine-3-carbonitrile \((2a)\)

A stirred solution of 1a \((0.1 \text{ g}, 0.225 \text{ mmol})\), 2-cyano-N-(4-methoxyphenyl)acetamide \((0.057 \text{ g}, 0.3 \text{ mmol})\), HOAc \((0.03 \text{ mL})\) and piperidine (0.017 mL) in toluene \((4 \text{ mL})\) was refluxed for 3 h. The solvent was evaporated and the residue was purified by column chromatography (toluene–EtOAc, 1:1; yield: 0.065 g \((47\%)\), yellowish syrup; $\text{R} _f$ 0.54 (toluene–EtOAc, 1:1); $[\alpha]_{D}^{23} -53.9 \left( c = 1, \text{ CHCl}_3 \right)$.\(^1\)\(^7\)
### Table 1: ¹H NMR Data for Compounds 2a, 2b, 3a, 3b, 4 and 5

<table>
<thead>
<tr>
<th>Compound</th>
<th>Chemical Structure</th>
<th>δ (ppm)</th>
<th>J (Hz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2a</td>
<td><img src="image1" alt="Structure" /></td>
<td>2.47 (br, 1 H, 3'-OH), 3.44 (dd, 1 H, 1H)</td>
<td>2.8 Hz, 7.6 Hz</td>
</tr>
<tr>
<td>2b</td>
<td><img src="image2" alt="Structure" /></td>
<td>2.35 (br, 1 H, 3'-OH), 3.46 (dd, 1 H, J = 2.7 Hz)</td>
<td>7.6 Hz</td>
</tr>
<tr>
<td>3a</td>
<td><img src="image3" alt="Structure" /></td>
<td>2.33 (br, 3'-OH), 3.56 (dd, 1 H, J = 2.7 Hz)</td>
<td>7.6 Hz</td>
</tr>
<tr>
<td>3b</td>
<td><img src="image4" alt="Structure" /></td>
<td>2.46 (br, 1 H, 3'-OH), 3.52 (dd, 1 H, J = 2.7 Hz)</td>
<td>6.8 Hz</td>
</tr>
<tr>
<td>4</td>
<td><img src="image5" alt="Structure" /></td>
<td>2.41 (br, 1 H, 3'-OH), 3.54 (dd, 1 H, J = 2.7 Hz)</td>
<td>6.8 Hz</td>
</tr>
<tr>
<td></td>
<td><img src="image6" alt="Structure" /></td>
<td>3.22 (s, 3H, OCH₃), 3.56 (m, 2 H, H₂-6)</td>
<td>8.0 Hz</td>
</tr>
<tr>
<td></td>
<td><img src="image7" alt="Structure" /></td>
<td>2.84 (br, 1 H, OH), 3.72 (dd, 1 H, J = 2.7 Hz)</td>
<td>9.2 Hz</td>
</tr>
</tbody>
</table>

* At 300.13 MHz.

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IR (film): 3462 (OH), 2227 (C=O), 1668 cm⁻¹ (C=O).

MS (CI isobutane): m/z (%) = 617 (20, M⁺), 509 (11, M - OCH₃Ph⁺), 91 (100).

Anal. Calcd. for C₁₅H₁₄O₅N₂ (616.7): C, 74.01; H, 5.88; N, 4.54. Found: C, 74.16; H, 5.71; N, 4.78.

IR (film): 3457 (OH), 2228 (C=O) 1669 cm⁻¹ (C=O).

MS (CI isobutane): m/z (%) = 617 (17, M⁺), 509 (2, M - OCH₃Ph⁺), 91 (100).

Anal. Calcd. for C₁₅H₁₄O₅N₂ (616.7): C, 74.01; H, 5.88; N, 4.54. Found: C, 73.82; H, 6.14; N, 4.38.

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**Chemical Structures**

2-(2,3,4-Tri-O-benzyl-1-hyroxy-1,2,3,4-tetrahydroxybutyl)-1,2-dihydro-1-(4-methoxy phenyl)-2-oxopyridine-3-carbonitrile (2b) The reaction of 1b was carried out as described for 2a: yield: 0.077 g (56%); yellow syrup; R₀ 0.16 (toluene-EtOAc, 3:1); [°α]D² = +48.3 (c = 1, CHCl₃).

IR (film): 3457 (OH), 2228 (C=O) 1669 cm⁻¹ (C=O).

MS (CI isobutane): m/z (%) = 617 (17, M⁺), 509 (2, M - OCH₃Ph⁺), 91 (100).

Anal. Calcd. for C₁₅H₁₄O₅N₂ (616.7): C, 74.01; H, 5.88; N, 4.54. Found: C, 73.82; H, 6.14; N, 4.38.

**Chemical Structures**

2-(2,3,4-Tri-O-benzyl-1-hyroxy-1,2,3,4-tetrahydroxybutyl)-benzol[4,5]imidazo[1,2-a]pyridine-4-carbonitrile (3a) Compound 1a (0.1 g, 0.225 mmol) was reacted with 2-benzimidazolodiacetic acid (0.047 g, 0.3 mmol) as described for 2a. The reaction was stirred under reflux for 1 h. The solvent was removed and the residue was purified by column chromatography (toluene-EtOAc, 2:1); yield: 0.066 g (50%); yellow solid; mp 67–69 °C (n-heptane-CH₂Cl₂); Rₐ 0.30 (toluene–EtOAc–2:1); [α]D² = -39.8 (c = 1, CHCl₃).

IR (KBr): 3420 (OH), 2231 (C=O), 1635 cm⁻¹ (C=C).

MS (70 eV): m/z (%) = 584 (5, M⁺), 90 (100).


IR (KBr): 3386 (OH), 2232 (C=O), 1637 cm⁻¹ (C=C).

MS (CI isobutane): m/z (%) = 584 (60, M⁺), 476 (13, M - OCH₃Ph⁺), 91 (100).

Table 2 13C NMR Data for Compounds 2a, 2b, 3a, 3b, 4, 5 and 6

<table>
<thead>
<tr>
<th>Product</th>
<th>13C NMR δ (62.9 MHz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2a</td>
<td>55.6 (OCH3), 69.8 (C-3'), 70.6 (C-4'), 72.1, 73.6, 74.1 (CH2Ph), 76.5 (C-1'), 80.5 (C-2'), 105.7 (C-3), 114.5 (m-NC6H4) 115.4 (CN), 116.6 (C-5), 127.0 (o-NC6H4), 128.1, 128.2, 128.4 (CH2, CH2), 128.3, 128.5 (2 × C), 128.6 (CH3, CH3), 132.2 (i-NC6H4), 133.8, 133.8, 137.3 (C, C6H5), 141.8 (C-6), 148.2 (C-4), 159.1, 159.8 (p-NC6H4, C-2)</td>
</tr>
<tr>
<td>2b</td>
<td>55.6 (OCH3), 69.1 (C-3'), 70.9 (C-4'), 71.6, 73.6, 74.6 (CH2Ph), 77.0 (C-1'), 80.0 (C-2'), 106.0 (C-3), 114.5 (m-NC6H4), 115.4 (CN), 116.9 (C-5), 127.0 (o-NC6H4), 128.0-128.6 (CH3, CH3), 132.1 (i-NC6H4), 136.7, 136.8, 137.5 (C12, C12), 142.3 (C-6), 146.4 (C-4), 159.1, 159.8 (p-NC6H4, C-2)</td>
</tr>
<tr>
<td>3a</td>
<td>69.8 (C-3'), 70.5 (C-4'), 72.2, 73.6, 74.2 (CH2Ph), 76.7 (C-1'), 80.6 (C-2'), 101.6 (C-4), 110.8 (C-9), 114.8 (CN), 120.6 (C-6), 121.2 (C-2), 122.4 (C-8), 126.9 (C-7), 128.0, 128.2 (2 × C), 128.5, 128.6 (2 × C), 128.85 (CH3, CH3), 128.1, 128.4, 128.5 (CH3, CH3), 128.3 (C-1), 128.3 (C-9a), 136.4 (C-3), 136.3, 136.7, 137.4 (C6, C6), 144.5 (C-5a), 145.0 (C-4a)</td>
</tr>
<tr>
<td>3b</td>
<td>69.1 (C-3'), 70.9 (C-4'), 71.8, 73.7, 74.7 (CH2Ph), 77.3 (C-1'), 80.3 (C-2'), 101.9 (C-4), 110.7 (C-9), 114.8 (CN), 120.7 (C-6), 121.5 (C-2), 122.4 (C-8), 126.9 (C-7), 128.0 (2 × C), 128.1 (2 × C), 128.3, 128.6 (CH3, CH3), 128.0, 128.2, 128.5 (CH3, CH3), 128.5 (C-1), 128.6 (C-9a), 136.2 (C-3), 136.2, 136.7, 137.6 (C6, C6), 144.6 (C-5a), 145.1 (C-4a)</td>
</tr>
<tr>
<td>4a</td>
<td>69.2 (C-3'), 71.0 (C-4'), 72.0, 73.7, 74.8 (CH2Ph), 77.4 (C-1'), 80.5 (C-2'), 110.6 (C-9), 120.5 (C-2), 121.3 (C-6), 122.9 (C-8), 127.2 (C-7), 127.9, 128.0, 128.2 (CH2, CH2), 128.1, 128.2, 128.3 (2 × C), 128.6 (2 × C), 128.8 (2 × C), 128.2, 128.5 (C-4, 9a), 136.0 (C-1), 136.3, 136.7, 137.6 (C6, C6), 140.1 (C-4a), 145.2 (C-5a)</td>
</tr>
<tr>
<td>5</td>
<td>45.5 (C-2'), 55.2 (OCH3), 69.2 (C-6'), 69.9 (C-5'), 71.6, 73.6, 74.6 (CH2Ph), 71.7 (C-4'), 77.5 (C-3'), 99.4 (C-1'), 108.9 (C-2), 115.0 (CNO), 123.7 (br, C-5', C-6'), 127.5–128.5 (CH2, CH2), 137.7, 137.9, 138.4 (C6, C6), 141.5 (C-2'), 150.4 (C-3), 152.3' (C-4'), C-7' and C-7'α are not given due to strong signal broadening. In DMSO-d6: δ = 111.7 (C-4'), 119.5 (C-7'), 122.4 (C-5'), 123.8 (C-6'), 134.8 (C-3'a'), 143.4 (C-7'a')</td>
</tr>
<tr>
<td>6a</td>
<td>55.4 (CH3), 74.5 (C-4'), 77.8 (C-3'), 78.5 (C-2'), 69.6 (C-1'), 104.4 (C-3), 114.6 (m-NC6H4), 116.2, 116.4 (CN, C-5), 128.0 (o-NC6H4), 133.5 (m-NC6H4), 143.0 (C-6), 149.0 (C-4), 159.6, 160.2 (p-NC6H4, C-2)</td>
</tr>
</tbody>
</table>

*At 75.5 MHz.

2-(1,2,4,5-tetrahydroxybutyl)-4-nitrobenzo[4,5]imidazol[1,2-a]pyridine (4)
Compound 1a (0.1 g, 0.225 mmol) was reacted with 2-nitromethylbenzimidazole (0.053 g, 0.3 mmol) as described for 3b. After 1 h, another portion of 2-nitromethylbenzimidazole (0.053 g, 0.3 mmol) was added. The mixture was stirred under reflux for another 3 h. The solvent was evaporated and the residue was purified by column chromatography (toluene-EtOAc, 1:1; yield: 0.082 g (60%); orange crystals; mp 159–162 °C (toluene–n-heptane); Rf 0.37 (toluene–EtOAc, 1:1); [α]D20 = −17.9 (c = 1, CHCl3).

IR (KBr): 3264 (OH), 1651 (C=C), 1363 cm⁻¹ (NO2).

MS (Cl isobutane): m/z (%) = 604 (36, M+H+), 574 (58, M – NO+), 496 (10, M – OCH2Ph), 91 (100).

Anal. Calc. for C31H31N3O4: C, 73.06; H, 6.13; N, 8.25. Found: C, 72.87; H, 5.94; N, 8.29.

1,2-Dihydro-5-(1-arabino-1,2,3,4-tetrahydroxybutyl)-1-(4-methoxyphenyl)-2-oxopyridine-3-carbonitrile (6)
Compound 2a (200 mg, 0.324 mmol) was dissolved in CHCl3 (5 mL). At 25 °C idotrimethylsilane (0.260 mL, 1.944 mmol) was added and the mixture was stirred under argon for 20 h at r.t. It was then treated with MeOH (10 mL) and stirred for 5 h at r.t. After removal of the solvent, the residue was dissolved in CHCl3 (15 mL). The solution was washed with a sat. solution of Na2SO4 (15 mL) and H2O (2×15 mL). The combined aqueous phases were extracted with EtOAc (4 × 15 mL) and the organic phases were dried (Na2SO4). After evaporation of the solvent, the residue was purified by column chromatography (CHCl3–MeOH, 7:1); yield: 44 mg (39%); colorless syrup; Rf 0.29 (CHCl3–MeOH, 7:1); [α]D20 +62.9 (c = 0.16, acetone).

IR (KBr): 2230 cm⁻¹ (CN). MS (70 eV): m/z (%) = 328 (41, M – H2O). HRMS: m/z Calcd for C31H31N3O4H2O: 328.10593. Found: 328.10580.

Acknowledgements
The authors would like to thank the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for financial support. A. M. is grateful to the Deutscher Akademischer Austauschdienst for a scholarship.
References

(1) Presented at the XXth International Carbohydrate Symposium, Hamburg, Germany, 2000.
(9) Remy, R. J.; Secrist, J. A. Nucleosides Nucleotides 1985, 4, 411.