C-Branched Glycals as Monosaccharidic Push-Pull Butadienes*

Ivo Rudloff[a,b], Ahmed Bari[a], Holger Feist[a], Manfred Michalik[c], Helmut Reinke[a], and Klaus Peseke[a]

[a] Fachbereich Chemie, Universität Rostock, Albert-Einstein-Straße 3a, D-18051 Rostock
[b] Oswel/Eurogentec SA, Winchester Hill Commercial Park, Winchester Hill, Romsey, Hampshire, SO51 7UT, UK
[c] Leibniz-Institut für Organische Katalyse, Buchbinderstraße 5-6, D-18055 Rostock

Reprint requests to Prof. Dr. K. Peseke. Fax +49(381)4986412.
E-mail: klaus.peseke@chemie.uni-rostock.de

Z. Naturforsch. **59b,** 398 – 405 (2004); received January 8, 2004

Dedicated to Dr. Eckehard Cuny on the occasion of his 60th birthday

Treatment of 2(3)-formyl-glycals **1**, **3**, **5** with alkyl cyanoacetates afforded 2(3)-[(*E*)-2-cyano-2-alkoxycarbonyl-vinyl]-2(3)-deoxy-1,5(2, 6)-anhydro-hex-1(2)-enitols **2**, **4**, **6** which were reacted with aniline to yield nicotinonitrile acyclo-*C*-nucleosides **7**, **9**. Nicotinic acid ester acylo-*C*-nucleosides **11** were obtained by the reaction of 2,6-anhydro-1,4,5-tri-*O*-benzyl-3-[(*E*)-2-cyano-2-alkoxycarbonyl-vinyl]-3-deoxy-D-*erythro*-hex-2-enitols **6** with ammonia.

Key words: *C*-Nucleoside Analogues, Pyridines, 1,2-Dihydropyridin-2-ones, Nicotinic Acid Esters, Nicotinonitrile

Introduction

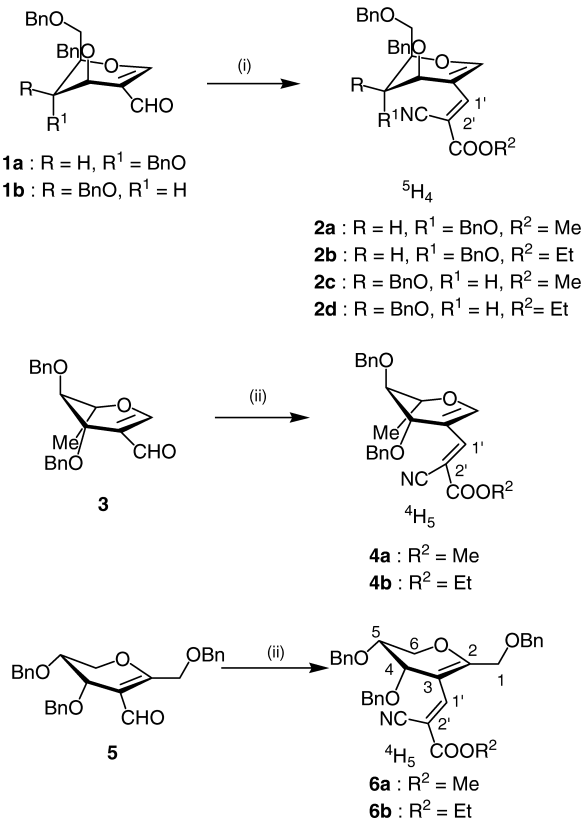
Only a few methods for the synthesis of C-2 branched glycals are known [1 – 4]. Ramesh and Balasubramanian carried out a formylation of *O*-methyl and *O*-benzyl protected glycals with *N*,*N*-dimethylformamide and $POCl_3$ to yield the 2-formyl-glycals **1a**, **1b** [5]. We adapted this Vilsmeier-Haack reaction to di-*O*-benzyl-L-rhamnal and tri-*O*-benzyl-D-fructal to furnish the corresponding formylglycals **3** and **5** [6]. Earlier own studies showed that Knoevenagel compounds derived from aromatic carbonyl compounds with an active methylene group in the neighborhood of electron-withdrawing activated C-C double bond reacted with carbon disulfide and alkyl halides in the presence of bases to afford push-pull butadienes with their characteristic unsymmetrical arrangement of donor and acceptor substituents [7, 8]. Push-pull butadienes are interesting building blocks for the synthesis of heterocyles [9, 10]. Here we report the syntheses of C-2(3) branched-chain glycals with an integrated push-pull butadiene structure unit, that could allow a displacement reaction of pyranose ring oxygen with *N*-nucleophiles resulting in a ring transformation triggered by an attack on the ester or nitrile group, respectively. In this way, in continuation of our investigations on the preparation of acyclic *C*-nucleoside analogues [11 – 14] we realized the synthesis of substituted 1,2-dihydropyridin-2-ones and nicotinic acid esters, respectively, with an alditol unit.

1,2-Dihydropyridin-2-ones have unique activity towards resistant *E. coli* DNA gyrase and topoisomerase IV [15]. Furthermore, 1,2-dihydropyridin-2-ones showed 5-HT_{1A}/5-HT_{2A} and HIV activity [16, 17].

Results and Discussion

1,5-Anhydro-3,4,6-tri-*O*-benzyl-2-deoxy-2-formyl-D-*arabino*-hex-1-enitol **1a** was treated with methyl and ethyl cyanoacetate, respectively, to give the monosaccharidic butadienes **2a** and **2b** as colorless crystals. These reactions were performed by using piperidinium acetate as the most efficient catalyst in boiling toluene. For a complete conversion of **1**, **3** and **5** into the corresponding Knoevenagel compounds **2**, **4**, **6** the use of refluxing chlorobenzene as solvent was necessary. In addition, a longer reaction time for the reaction of 2,6-anhydro-1,4,5-tri-*O*-benzyl-3-deoxy-

* Presented in part at the 6th Conference on Iminium Salts (ImSaT-6), Stimpfach-Rechenberg (Germany), September 16 – 18, 2003.



Scheme 1. (i) $CH_2(CN)COOR^2$ (R^2 = Me, Et), piperidinium acetate, toluene or chlorobenzene, reflux; (ii) $CH_2(CN)COOR^2$ (R^2 = Me, Et), piperidinium acetate, chlorobenzene, reflux.

3-*C*-formyl-D-*erythro*-hex-2-enitol (**5**) with methyl and ethyl cyanoacetate was required. This may be attributed to the steric hindrance towards a nucleophilic attack on the formyl group in compound **5**.

The NMR spectra of **2**, **4**, **6** showed the existence of only one diastereomer. With gated decoupling spectra it could be proved that the *E*-isomers were obtained in all cases [18, 19]. We found a large coupling constant ($J = 13.4$ Hz) for the coupling between the nitrile carbon and 1'-H at the exocyclic double bond. On the other hand, there is a smaller value ($J = 6.8$ Hz) for the coupling between the ester carbonyl carbon and 1'-H.

The conformations of compounds **2**, **4** and **6** were confirmed by the couplings found over four bonds between 3-H and 5-H (in the case of **2** and **4**) and 4-H and 6-H (in the case of **6**), respectively, due to the *W*-coupling. The values of these coupling constants (1.5 – 2.5 Hz) are possible only if the protons are arranged equatorially.

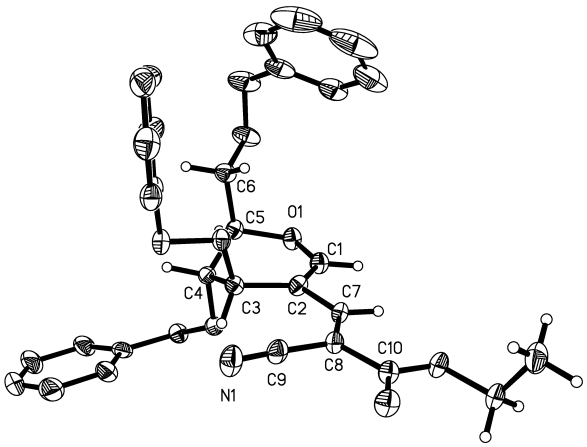


Fig. 1. ORTEP drawing of **2b** (hydrogens omitted for clarity).

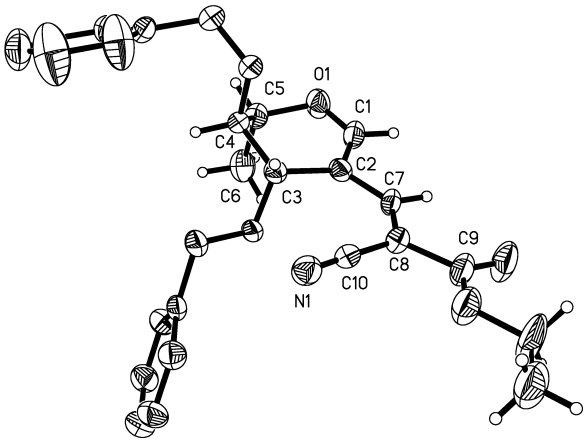
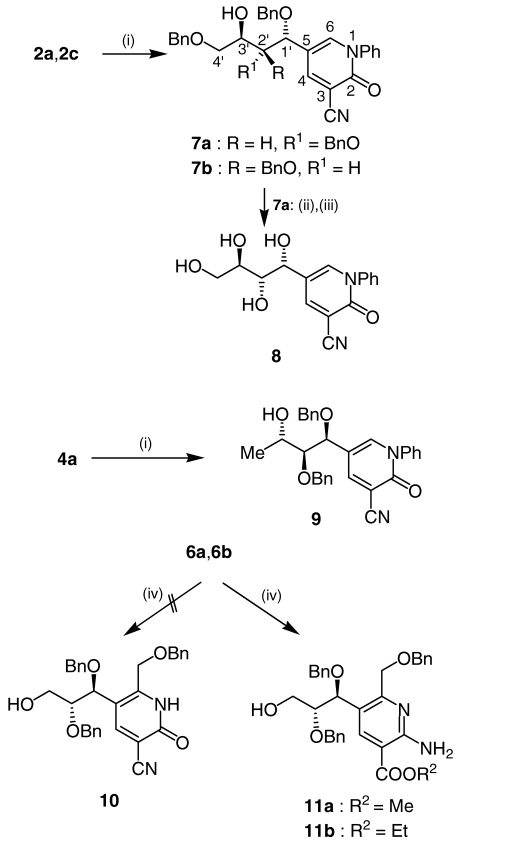


Fig. 2. ORTEP drawing of **4b** (hydrogens omitted for clarity).

Furthermore, the *E*-configuration of **2b** and **4b** was proved by X-ray structure analysis. In order to obtain best possible results the data collection of **2b** was carried out at 223 K. ORTEP drawings of **2b** with 30% probability of the thermal ellipsoids and of **4b** with 25% probability of the thermal ellipsoids are shown in Figures 1 and 2, which include also the numbering scheme of the most important atoms.

The crystallographic data are in agreement with the $^5H_4$-conformation for compound **2b** and the $^4H_5$-conformation for compound **4b**. Furthermore, the *s-trans* arrangement of the butadiene subunit is confirmed. A complete conjugation in the π system caused a planar arrangement of this part of the molecule between O(1) and C(9) and between O(1) and C(10), respectively. The reduced bond length of O(1)-C(1) (133.4 pm in **2b** and 133.1 pm in **4b**) and C(2)-C(7)



Scheme 2. (i) Aniline, EtOH, reflux; (ii) Me_3SiI, $CHCl_3$, r. t., 20 h; (iii) MeOH, r. t., 5 h; (iv) NH_3, EtOH, reflux.

(143.3 pm in **2b** and 142.7 pm in **4b**) showed the push-pull butadiene character. In both structures the single bond O(1)-C(1) is shorter than the endocyclic double bond. On the other hand, the enlargement of the double bonds C(1)-C(2) (134.1 pm in **2b** and 133.8 pm in **4b**) and C(7)-C(8) (136.2 pm in **2b** and 133.2 pm in **4b**) was not as high as expected [20, 21].

Both bond lengths and carbon chemical shifts of the butadiene fragment determined for the compounds **2b** and **4b** indicate a strong electrophilic activation of the C-1 atom. Thus, the treatment of 2-[(*E*)-2-cyano-2-methoxycarbonyl-vinyl]glycals **2a**, **2c** and **4a** with aniline in boiling EtOH resulted in the formation of 1,2-dihydro-2-oxo-1-phenyl-pyridine-3-carbonitriles **7a,b** and **9**. The nucleophilic attack of aniline at C-1 of compounds **2a**, **2c** and **4a** would be expected to result in the following cyclization reaction under participation of the carbalkoxy group.

The IR spectra of the isolated compounds proved the existence of a cyano group. Furthermore, there were also absorptions which are typical for amides. The corresponding mass spectra showed the expected molecular peaks for the products.

Catalytic hydrogenation of compound **7a** was not successful because of the presence of nitrile group. Therefore, iodotrimethylsilane was used for the removal of benzyl protecting groups [22, 23].

The reaction took 20 h to complete and was followed by the addition of methanol to the reaction mixture to afford the 1,2-dihydro-5-(D-*arabino*-1,2,3,4-tetrahydroxybutyl)-1-phenyl-2-oxo-pyridine-3-carbonitrile (**8**).

Surprisingly, the treatment of 2,6-anhydro-1,4,5-tri-*O*-benzyl-3–[(*E*)–2-cyano-2-alkoxycarbonyl-vinyl]-3-deoxy-D-*erythro*-hex-2-enitols (**6a** and **6b**) with aniline under the described conditions failed. However, **6a** and **6b** reacted with ammonia in EtOH at ambient temperature to furnish the alkyl 2-amino-6-benzyloxymethyl-5-(1,2-di-*O*-benzyl-D-*erythro*-1,2,3-trihydroxy-propyl)pyridine-3-carboxylates **11a** and **11b** in excellent yields. In contrast to the above described conversion with aniline the reaction with ammonia proceeded through a nitrile cyclization to yield the corresponding nicotinic acid esters. The IR spectra showed typical absorptions for NH_2 and the ester group, but no cyano band was found. Furthermore, in the ^{13}C NMR spectra the signal for C-2 of the pyridine (the former nitrile carbon atom) was shifted downfield and found at $\delta = 160.1$ for **11a** and $\delta = 159.6$ for **11b**. The formation of the dihydronicotinonitrile **10** was not observed.

Experimental Section

General procedures

Solvents were distilled and if necessary dried using standard procedures. TLC was carried out on silica gel 60 GF_{254} (Merck) with detection by UV light ($\lambda = 254$ nm) and/or by charring with 10% sulfuric acid in methanol. Silica gel 60 (63 – 200 mesh) (Merck) was used for column chromatography. Melting points were determined by using a Boetius melting point apparatus and are corrected. Specific rotations were determined with a Polar LμP (IBZ Messtechnik). IR spectra were recorded with a Nicolet 205 FT-IR spectrometer. ^1H NMR spectra (250.13 MHz and 300.13 MHz, respectively) and ^{13}C NMR spectra (62.9 MHz and 75.5 MHz, respectively) were recorded on Bruker instruments AC 250 and ARX 300, with $CDCl_3$ (compound **8** with [D_6]-DMSO) as solvent. The calibration of spectra was carried out on solvent signals ($\delta(^1H, CDCl_3) = 7.25$; $\delta(^{13}C, CDCl_3) = 77.0$; [$D_6$]-DMSO: $\delta(^1H) = 2.50$; $\delta(^{13}C) = 39.7$). The ^1H

and ^{13}C NMR signals were assigned by DEPT and two-dimensional ^{1}H,^{1}H-COSY and ^{1}H,^{13}C correlation spectra. The mass spectra were recorded on an AMD 402/3 spectrometer (AMD Intectra GmbH). Elemental analyses were performed on a Leco CHNS-932 instrument.

*1,5-Anhydro-3,4,6-tri-O-benzyl-2-[(E)-2-cyano-2-methoxycarbonyl-vinyl]-2-deoxy-D-arabino-hex-1-enitol (**2a**)*

A solution of **1a** (1.50 g, 3.30 mmol), methyl cyanoacetate (0.30 ml, 3.30 mmol), acetic acid (0.1 ml, 1.7 mmol) and piperidine (0.05 ml, 0.51 mmol) in toluene (20 ml) was heated for 30 min at reflux using a Dean-Stark trap for 30 min. After removal of solvent the residue was dissolved in MeOH for crystallization overnight. Yield 1.28 g (72%), colorless crystals. – M. p. 138 – 140 °C (MeOH). – $[\alpha]_D^{22} = +20.6°$ (*c* 1, $CHCl_3$). – $R_f = 0.78$ (toluene/ethyl acetate 5:2). – IR (KBr): $\nu = 2216$ (CN), 1702 (C=O), 1590 (C=C) cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 3.50$ (dd, 1H, $^{2}J_{6a,6b} = 10.6$ Hz, $^{3}J_{5,6a} = 5.2$ Hz, 6a-H), 3.67 (dd, 1H, $^{3}J_{5,6b} = 7.5$ Hz, 6b-H), 3.76 (s, 3H, OCH_3), 4.03 (t, 1H, $^{3}J_{3,4} \approx {}^{3}J_{4,5} = 2.3$ Hz, 4-H), 4.31 (d, 1H, $^{2}J = 12.0$ Hz, C*H*HPh), 4.36 (d, 1H, $^{2}J = 10.4$ Hz, C*H*HPh), 4.37 (d, 1H, $^{2}J = 12.0$ Hz, C*H*HPh), 4.58 (m, 2H, center of an AB quartet, C*H*$_2$Ph), 4.65 (m, 1H, 5-H), 4.75 (t, 1H, $^{3}J_{3,4} = {}^{4}J_{3,5} = 2.3$ Hz, 3-H), 4.78 (d, 1H, $^{2}J = 10.4$ Hz, C*H*HPh), 7.10 – 7.26 (m, 16H, 1-H, Ph), 7.61 (s, 1H, 1'-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta = 52.9$ (OCH_3), 67.8 (C-3), 68.1 (C-6), 68.4 (C-4), 69.7, 71.7, 73.4 (3 × *C*H$_2$Ph), 78.1 (C-5), 95.2 (C-2'), 111.5 (C-2), 116.6 (CN), 127.7 – 128.7 (*o*-, *m*-, *p*-Ph), 137.0, 137.5, 137.5 (3 × *i*-Ph), 154.7 (C-1'), 160.6 (C-1), 164.1 (C=O). – MS (CI, *iso*-butane): m/z (%) = 526 (22) (MH^+), 418 (100) ($M\text{-}OCH_2Ph^+$). – $C_{32}H_{31}NO_6$ (525.59): calcd. C 73.13, H 5.94, N 2.66; found C 72.91, H 5.92, N 2.74.

*1,5-Anhydro-3,4,6-tri-O-benzyl-2-[(E)-2-cyano-2-ethoxycarbonyl-vinyl]-2-deoxy-D-arabino-hex-1-enitol (**2b**)*

Compound **1a** (1.50 g, 3.30 mmol) reacted with ethyl cyanoacetate (0.35 ml, 0.35 ml, 3.30 mmol) as described for preparation of **2a**. Yield 1.26 g (69%); colorless crystals. – M. p. 116 °C (MeOH). – $[\alpha]_D^{24} = +22.0°$ (*c* 1, $CHCl_3$). – $R_f = 0.80$ (toluene/ethyl acetate 5:2). – IR (nujol): $\nu = 2218$ (CN), 1718 (C=O), 1585 (C=C) cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 1.26$ (t, 3H, $^{3}J = 7.1$ Hz, CH_3), 3.50 (dd, 1H, $^{2}J_{6a,6b} = 10.7$ Hz, $^{3}J_{5,6a} = 5.2$ Hz, 6a-H), 3.67 (dd, 1H, $^{3}J_{5,6b} = 7.5$ Hz, 6b-H), 4.10 (t, 1H, $^{3}J_{3,4} = {}^{3}J_{4,5} = 2.4$ Hz, 4-H), 4.23 (q, 2H, COOC*H*$_2$), 4.30 (d, 1H, $^{2}J = 12.0$ Hz, C*H*HPh), 4.36 (d, 1H, $^{2}J = 10.4$ Hz, C*H*HPh), 4.37 (d, 1H, $^{2}J = 12.0$ Hz, C*H*HPh), 4.58 (m, 2H, center of an AB quartet, C*H*$_2$Ph), 4.65 (m, 1H, 5-H), 4.76 (t, 1H, $^{3}J_{3,4} = {}^{4}J_{3,5} = 2.4$ Hz, 3-H), 4.79 (d, 1H, $^{2}J = 10.4$ Hz, C*H*HPh), 7.10 – 7.32 (m, 16H, 1-H, Ph), 7.61 (s, 1H, 1'-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta = 14.2$ (CH_3), 62.0 (COO*C*H$_2$), 67.9 (C-6), 68.2, 68.5 (C-3, C-4), 69.8, 71.7, 73.4 (3 × *C*H$_2$Ph), 78.0 (C-5), 95.7 (C-2'), 111.4 (C-2), 116.5 (CN), 127.6 – 128.7 (*o*-, *m*-, *p*-Ph), 137.0, 137.5, 137.5 (3 × *i*-Ph), 154.4 (C-1'), 160.3 (C-1), 163.5 (C=O). – MS (EI, 70 eV): m/z (%) = 539 (8) (M^+). – $C_{33}H_{33}NO_6$ (539.62): calcd. C 73.45, H 6.16, N 2.60; found C 73.29, H 6.29, N 2.57.

*1,5-Anhydro-3,4,6-tri-O-benzyl-2-[(E)-2-cyano-2-methoxycarbonyl-vinyl]-2-deoxy-D-lyxo-hex-1-enitol (**2c**)*

1b reacted with methyl cyanoacetate in chlorobenzene as described for the preparation of **2a**. After removal of the solvent the residue was purified by column chromatography (toluene/ethyl actetate 9:1). Yield 1.05 g (59%); colorless syrup. – $[\alpha]_D^{22} = +36.0°$ (*c* 1, $CHCl_3$). – $R_f = 0.38$ (toluene/ethyl acetate 9:1). – IR (nujol): $\nu = 2219$ (CN), 1724 (C=O), 1582 (C=C) cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 3.75$ (s, 3H, OCH_3), 3.85 – 3.98 (AB part of ABX, 2H, $^{2}J_{6a,6b} = 11.3$ Hz, $^{3}J_{6a,5} = 7.5$ Hz, $^{3}J_{6b,5} = 3.5$ Hz, 6a-H, 6b-H), 4.00 (dd, 1H, $^{3}J_{4,3} = 3.3$ Hz, $^{3}J_{4,5} = 4.3$ Hz, 4-H), 4.37 (d, 1H, $^{2}J = 12.0$ Hz, C*H*HPh), 4.48 – 4.60 (m, 3H, 5-H, 2 × C*H*HPh), 4.72 (d, 1H, $^{2}J = 12.0$ Hz, C*H*HPh), 4.85 – 4.95 (m, 3H, 3-H, 2 × C*H*HPh), 7.15 – 7.30 (16H, 1-H, Ph), 7.59 (s, 1H, 1'-H). – ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 52.9$ (OCH_3), 68.1 (C-6), 68.3 (C-3), 72.2, 72.9, 73.5 (3 × *C*H$_2$Ph), 77.3 (C-4), 78.2 (C-5), 95.9 (C-2'), 112.8 (C-2), 116.5 (CN), 126.8 – 127.7 (*o*-, *m*-, *p*-Ph), 136.9, 137.4, 137.4 (3 × *i*-Ph), 153.3 (C-1'), 159.6 (C-1), 163.9 (C=O). – MS (CI, *iso*-butane): m/z (%) = 526 (37) (MH^+), 418 (100) ($M\text{-}OCH_2Ph^+$). – $C_{32}H_{31}NO_6$ (525.59): calcd. C 73.13, H 5.94, N 2.66; found C 72.86, H 6.09, N 2.72.

*1,5-Anhydro-3,4,6-tri-O-benzyl-2-[(E)-2-cyano-2-ethoxycarbonyl-vinyl]-2-deoxy-D-lyxo-hex-1-enitol (**2d**)*

1b reacted with ethyl cyanoacetate in chlorobenzene as described for the preparation of **2a**. After removal of the solvent the residue was purified by column chromatography (toluene/ethyl actetate 9:1). Yield 1.0 g (55%); colorless syrup. – $[\alpha]_D^{23} = +38.3°$ (*c* 1, $CHCl_3$). – $R_f = 0.4$ (toluene/ethyl acetate 9:1). – IR (capillary): $\nu = 2218$ (CN), 1718 (C=O), 1583 (C=C) cm^{-1}. – ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.28$ (t, 3H, $^{3}J = 7.1$ Hz, CH_3), 3.84 – 3.98 (AB part of ABX, 2H, $^{2}J_{6a,6b} = 11.3$ Hz, $^{3}J_{5,6a} = 7.5$ Hz, $^{3}J_{5,6b} = 3.5$ Hz, 6a-H, 6b-H), 4.04 (dd, 1H, $^{3}J_{3,4} = 3.3$ Hz, $^{3}J_{4,5} = 4.3$ Hz, 4-H), 4.24 (q, 2H, COOC*H*$_2$), 4.42, 4.50 ($q_{A,B}$, 2H, $^{2}J = 12.0$ Hz, C*H*$_2$Ph), 4.54 – 4.61 (m, 1H, 5-H), 4.61 (d, 1H, $^{2}J = 12.0$ Hz, C*H*HPh), 4.77 (d, 1H, $^{2}J = 12.0$ Hz, C*H*HPh), 4.91, 4.96 ($q_{A,B}$, 2H, $^{2}J = 10.8$ Hz, C*H*$_2$Ph), 4.95 (dd, 1H, $^{4}J_{3,5} = 1.5$ Hz, 3-H), 7.20 – 7.34 (m, 16H, 1-H, Ph), 7.63 (s, 1H, 1'-H). – ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 14.2$ (CH_3), 62.1 (COO*C*H$_2$), 68.0 (C-6), 68.2 (C-3), 72.1, 72.8,

73.5 (3 × CH_2Ph), 77.2 (C-4), 78.0 (C-5), 96.4 (C-2'), 112.7 (C-2), 116.5 (CN), 127.7 – 128.6 (*o*-, *m*-, *p*-Ph), 136.9, 137.4, 137.4 (3 × *i*-Ph), 153.0 (C-1'), 159.4 (C-1), 163.4 (C=O). – MS (CI, *iso*-butane): m/z (%) = 540 (22) (MH^+), 432 (100) (M-OCH_2Ph^+). – $C_{33}H_{33}NO_6$ (539.62): calcd. C 73.45, H 6.16, N 2.60; found C 73.20, H 5.98, N 2.65.

*1,5-Anhydro-3,4-di-O-benzyl-2-[(E)-2-cyano-2-methoxy-carbonyl-vinyl]-2,6-dideoxy-L-arabino-hex-1-enitol (**4a**)*

Compound **3** (1.50 g, 4.42 mmol) was treated with methyl cyanoacetate (0.44 g, 0.39 ml, 4.42 mmol) in chlorobenzene (20 ml) as described for the preparation of **2a**. After removal of the solvent the residue was purified by column chromatography (toluene/ethyl actetate 9:1). Yield 0.93 g (50%); colorless syrup. – $[\alpha]_D^{24} = +40.3°$ (*c* 1, $CHCl_3$). – $R_f = 0.49$ (toluene/ethyl acetate 9:1). – IR (capillary): ν = 2219 (CN), 1716 (C=O), 1584 (C=C) cm^{-1}. – ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.35$ (d, 3H, $^3J = 7.2$ Hz, CH_3), 3.78 (s, 3H, OCH_3), 3.82 (t, 1H, $^3J_{3,4} = {}^3J_{4,5} = 2.3$ Hz, 4-H), 4.42 (d, 1H, $^2J = 10.3$ Hz, C*H*HPh), 4.54 – 4.65 (m, 3H, 5-H, C*H*$_2$Ph), 4.80 (t, 1H, $^3J_{3,5} = 2.3$ Hz, 3-H), 4.85 (d, 1H, $^2J = 10.3$ Hz, C*H*HPh), 7.08 – 7.37 (m, 11H, 1-H, Ph), 7.65 (s, 1H, 1'-H). – ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 16.8 (CH_3), 52.8 (OCH_3), 68.5 (C-3), 69.6, 71.7 (2 × *C*H$_2$Ph), 71.4 (C-4), 75.7 (C-5), 94.7 (C-2'), 111.1 (C-2), 116.7 (CN), 127.8 – 128.7 (*o*-, *m*-, *p*-Ph), 137.1, 137.6, 137.6 (3 × *i*-Ph), 155.1 (C-1'), 160.8 (C-1), 164.2 (C=O). – MS (CI, *iso*-butane): m/z (%) = 420 (51) (MH^+), 312 (100) (M-OCH_2Ph^+). – $C_{25}H_{25}NO_5$ (419.47): calcd. C 71.43, H 6.19, N 3.33; found C 71.14, H 6.19, N 3.14.

*1,5-Anhydro-3,4-di-O-benzyl-2-[(E)-2-cyano-2-ethoxy-carbonyl-vinyl]-2,6-dideoxy-L-arabino-hex-1-enitol (**4b**)*

3 (1.50 g, 4.42 mmol) reacted with ethyl cyanoacetate (0.50 g, 0.47 ml, 4.42 mmol) in chlorobenzene (20 ml) as described for the preparation of **2a**. Yield 1.14 g (59%); colorless plates. – M. p. 104 – 105 °C (diethyl ether). – $[\alpha]_D^{24} = +42.7°$ (*c* 1, $CHCl_3$). – $R_f = 0.51$ (toluene/ethyl acetate 9:1). – IR (KBr): ν = 2217 (CN), 1716 (C=O), 1582 (C=C) cm^{-1}. – ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.26$ (t, 3H, $^3J = 7.1$ Hz, CH_2C*H*$_3$), 1.34 (d, 3H, $^3J = 7.2$ Hz, CH_3), 3.81 (t, 1H, $^3J_{3,4} = {}^3J_{4,5} = 2.5$ Hz, 4-H), 4.22 (q, 2H, C*H*$_2$CH$_3$), 4.42 (d, 1H, $^2J = 10.4$ Hz, C*H*HPh), 4.54 – 4.65 (m, 3H, 5-H, C*H*$_2$Ph), 4.80 (t, 2H, $^3J_{3,5} = 2.5$ Hz, 3-H), 4.85 (d, 1H, $^2J = 10.4$ Hz, C*H*HPh), 7.12 – 7.35 (m, 11H, 1-H, Ph), 7.64 (s, 1H, 1'-H). – ^{13}C NMR (75.5 MHz, $CDCl_3$) $\delta = 14.2$ (CH$_2$*C*H$_3$), 16.7 (CH_3), 61.9 (*C*H$_2$CH$_3$), 68.4 (C-3), 69.6 (*C*H$_2$Ph), 71.3 (C-4), 71.6 (2 × *C*H$_2$Ph), 75.6 (C-5), 95.2 (C-2'), 111.0 (C-2), 116.7 (CN), 127.7 – 128.6 (*o*-, *m*-, *p*-Ph), 137.1, 137.6, 137.6 (3 × *i*-Ph), 154.7 (C-1'), 160.6 (C-1), 163.6 (C=O). – MS (CI, *iso*-butane): m/z (%) = 434 (48) (MH^+), 326 (100) (M-OCH_2Ph^+). – $C_{26}H_{27}NO_5$ (433.50): calcd. C 72.06, H 6.28, N 3.23; found C 72.31, H 6.37, N 3.20.

*2,6-Anhydro-1,4,5-tri-O-benzyl-3-[(E)-2-cyano-2-methoxy-carbonyl-vinyl]-3-deoxy-D-erythro-hex-2-enitol (**6a**)*

Compound **5** (1.5 g, 0.33 mmol) reacted with methyl cyanoacetate (0.66 g, 0.6 ml, 6.60 mmol) for 2 h in chlorobenzene as described above for the preparation of **2a**. After 1 h another 0.33 g (0.3 ml, 3.30 mmol) methyl cyanoacetate were added. After removal of the solvent the residue was purified by column chromatography (toluene/ethyl actetate 9:1). Yield 0.95 g (53.7%); colorless syrup. – $[\alpha]_D^{23} = +109.7°$ (*c* 0.5, $CHCl_3$). – $R_f = 0.49$ (toluene/ethyl acetate 9:1). – IR (capillary): ν = 2218 (CN), 1724 (C=O), 1576 (C=C) cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 3.74$ (ddd, 1H, 5-H), 3.80 (s, 3H, CH_3), 4.00 (d, 1H, $^2J_{1a,1b} = 12.8$ Hz, 1a-H), 4.14 (ddd, 1H, $^3J_{5,6eq} = 4.5$ Hz, $^4J_{4,6eq} = 1.3$ Hz, 6eq-H), 4.24 (d, 1H, 1b-H), 4.33 (dd, 1H, $^2J_{6ax,6eq} = 10.2$ Hz, $^3J_{5,6ax} = 11.0$ Hz, 6ax-H), 4.46 (center of an AB quartet, 2H, C*H*$_2$Ph), 4.59 (d, 1H, $^2J = 12.0$ Hz, C*H*HPh), 4.72 (d, 1H, $^2J = 12.0$ Hz, C*H*HPh), 5.00 (s, 2H, C*H*$_2$Ph), 5.33 (dd, 1H, 4-H), 7.14 – 7.36 (m, 15 H, Ph), 8.17 (s, 1H, 1'-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$) $\delta = 53.0$ (CH_3), 64.0 (C-1), 66.5 (C-4), 67.7 (C-6), 71.8, 72.1, 73.6 (3 × C*H*$_2$Ph), 73.6 (C-5), 95.7 (C-2'), 110.5 (C-3), 116.5 (CN), 127.5 – 128.7 (Ph), 136.6, 137.3, 138.8 (3 × *i*-Ph), 151.2 (C-1'), 164.3 (C=O), 167.3 (C-2). – MS (CI, *iso*-butane): m/z (%) = 526 (4) (MH^+), 418 (24) (M-OCH_2Ph^+). – $C_{32}H_{31}NO_6$ (525.59): calcd. C 73.13, H 5.94, N 2.66; found C 72.82, H 5.84, N 2.82.

*2,6-Anhydro-1,4,5-tri-O-benzyl-3-[(E)-2-cyano-2-ethoxy-carbonyl-vinyl]-3-deoxy-D-erythro-hex-2-enitol (**6b**)*

Compound **5** reacted with ethyl cyanoacetate (0.74 g, 0.7 ml, 6.60 mmol) for 2 h in chlorobenzene as described above for the preparation of **6a**. After 1 h another 0.37 g (0.35 ml, 3.30 mmol) ethyl cyanoacetate were added. After removal of the solvent the residue was purified by column chromatography (toluene/ethyl actetate 9:1). Yield 1.4 g (65.9%), colorless syrup. – $[\alpha]_D^{23} = +100.4°$ (*c* 1, $CHCl_3$). – $R_f = 0.51$ (toluene/ethyl acetate 9:1). – IR (capillary): ν = 2216 (CN), 1748 (C=O), 1577 (C=C) cm^{-1}. – ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.27$ (t, 3H, $^3J = 7.0$ Hz, CH$_2$C*H*$_3$), 3.74 (ddd, 1H, 5-H), 4.00 (d, 1H, $^2J_{1a,1b} = 12.8$ Hz, 1a-H), 4.14 (ddd, 1H, $^3J_{5,6eq} = 4.5$ Hz, $^4J_{4,6eq} = 1.3$ Hz, 6eq-H), 4.24 (d, 1H, 1b-H), 4.24 (q, 2H, C*H*$_2$CH$_3$), 4.32 (dd, 1H, $^2J_{6ax,6eq} = 10.2$ Hz, $^3J_{5,6ax} = 11.0$ Hz, 6ax-H), 4.46 (center of an AB quartet, 2H, C*H*$_2$Ph), 4.58 (d, 1H, $^2J = 12.0$ Hz, C*H*HPh), 4.72 (d, 1H, $^2J = 12.0$ Hz, C*H*HPh), 5.00 (s, 2H, C*H*$_2$Ph), 5.33 (dd, 1H, 4-H), 7.12 – 7.34 (m, 15 H, Ph), 8.17 (s, 1H, 1'-H). – ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 14.2$

(CH_3), 62.1 (CH_2CH_3), 64.0 (C-1), 66.4 (C-4), 67.7 (C-6), 71.8, 72.1, 73.6 ($3 \times CH_2$Ph), 73.6 (C-5), 96.2 (C-2'), 110.4 (C-3), 116.7 (CN), 127.4 – 128.6 (*o*-, *m*-, *p*-Ph), 136.6, 137.3, 138.8 ($3 \times$ *i*-Ph), 150.9 (C-1'), 163.6 (C=O), 167.1 (C-2). – MS (CI, *iso*-butane): m/z (%) = 540 (28) (MH^+), 432 (96) ($M\text{-}OCH_2Ph^+$). – $C_{26}H_{27}NO_5$ (433.50): calcd. C 72.04, H 6.28, N 3.23; found C 71.78, H 6.02, N 3.48.

*5-(1,2,4-Tri-O-benzyl-D-arabino-1,2,3,4-tetrahydroxy-butyl)-1,2-dihydro-2-oxo-1-phenyl-pyridine-3-carbonitrile (**7a**)*

A solution of **2a** (1.0 g, 1.90 mmol) and aniline (0.53 g, 5.7 mmol) in EtOH (10 ml) was heated under reflux for 3 h. After the removal of the solvent the crude product was purified by column chromatography (chloroform/ethyl acetate 9:1). An additional purification was carried out by stirring with charcoal in dichloromethane at room temperature for 30 min. Yield 0.86 g (74.1%), yellowish syrup. $[\alpha]_D^{22} = -49.4°$ (*c* 1, $CHCl_3$). – $R_f = 0.75$ (chloroform/MeOH 9:1). – IR (capillary): $\nu = 3457$ (OH), 2228 (CN), 1663 (C=O) cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 2.43$ (d, 1H, $^3J = 7.0$ Hz, OH), 3.47 (dd, 1H, $^3J_{1',2'} = 3.0$ Hz, $^3J_{2',3'} = 7.6$ Hz, 2'-H), 3.56 – 3.66 (m, 2H, 4'a-H, 4'b-H), 3.93 (m, 1H, 3'-H), 4.18 (d, 1H, $^2J = 11.4$ Hz, C*H*HPh), 4.31 (d, 1H, $^2J = 12.0$ Hz, C*H*HPh), 4.41 (d, 1H, 1'-H), 4.45 (d, 1H, $^2J = 12.0$ Hz, C*H*HPh), 4.47 (s, 2H, CH_2Ph), 4.48 (d, 1H, $^2J = 11.4$ Hz, C*H*HPh), 7.00 – 7.42 (m, 21H, 4-H, Ph), 7.66 (d, 1H, $^4J_{4,6} = 2.5$ Hz, 6-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta = 69.9$ (C-3'), 70.6 (C-4'), 72.2, 73.7, 74.2 ($3 \times CH_2$Ph), 76.7 (C-1'), 80.6 (C-2'), 105.9 (C-3), 115.5 (CN), 117.0 (C-5), 126.0 – 129.5 (*o*-, *m*-, *p*-Ph), 137.2, 137.3, 137.6, 139.8 ($4 \times$ *i*-Ph), 141.5 (C-4), 147.2 (C-6), 159.0 (C=O). MS (CI, *iso*-butane): m/z (%) = 587 (60) (MH^+), 479 (38) ($M\text{-}OCH_2Ph^+$), 315 (18). – $C_{37}H_{34}N_2O_5$ (586.68): calcd. C 75.75, H 5.84, N 4.77; found C 75.47, H 5.64, N 4.62.

*5-(1,2,4-Tri-O-benzyl-D-lyxo-1,2,3,4-tetrahydroxy-butyl)-1,2-dihydro-2-oxo-1-phenyl-pyridine-3-carbonitrile (**7b**)*

2c (1.0 g, 1.90 mmol) reacted with aniline as described for the preparation of **7a**. Yield 0.82 g (70.7%); yellowish syrup. – $[\alpha]_D^{24} = +11.4°$ (*c* 0.5, $CHCl_3$). – $R_f = 0.725$ (chloroform/MeOH 9:1). – IR (capillary): $\nu = 3455$, 3366 (OH), 2228 (CN), 1664 (C=O) cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 2.30$ (d, 1H, $^3J = 8.0$ Hz, OH), 3.44 – 3.60 (m, 3H, 2'-H, 4'a-H, 4'b-H), 4.04 (m, 1H, 3'-H), 4.17 (d, 1H, $^2J = 11.3$ Hz, C*H*HPh), 4.24 (d, 1H, $^3J_{1',2'} = 8.0$ Hz, 1'-H), 4.35 (d, 2H, center of an AB quartet, $^2J = 11.6$ Hz, CH_2Ph), 4.40 – 4.51 (m, 3H, d, $^2J = 11.3$ Hz, AB quartet, $^2J = 11.6$ Hz)($3 \times$ C*H*HPh), 6.95 – 7.40 (m, 21H, 4-H, Ph), 7.69 (d, 1H, $^4J_{4,6} = 2.5$ Hz, 6-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta = 70.0$ (C-3'), 70.7 (C-4'), 72.2, 73.7, 74.2 ($3 \times CH_2$Ph), 76.9 (C-1'), 80.6 (C-2'), 105.9 (C-3), 115.5 (CN), 117.0 (C-5) , 126.1 – 129.5 (*o*-, *m*-, *p*-Ph), 137.2, 137.2, 137.5, 139.8 ($4 \times$ *i*-Ph), 141.7 (C-4), 147.4 (C-6), 159.0 (C=O). – MS (CI, *iso*-butane): m/z (%) = 587 (100) (MH^+), 479 (27) ($M\text{-}OCH_2Ph^+$), 315 (18). – $C_{37}H_{34}N_2O_5$ (586.68): calcd. C 75.75, H 5.84, N 4.77; found C 75.50, H 5.64, N 5.03.

*1,2-Dihydro-5-(D-arabino-1,2,3,4-tetrahydroxybutyl)-2-oxo-1-phenyl-pyridine-3-carbonitrile (**8**)*

To a vigorously stirred solution of **7a** (370 mg, 0.6 mmol) in $CHCl_3$ (10 ml) was added iodotrimethylsilane (0.5 ml, 3.5 mmol) and the mixture was stirred under argon for 20 h at room temperature. Methanol (10 ml) was added and the mixture was stirred for further 1 h. After removal of solvent the residue was dissolved in $CHCl_3$ (50 ml) and washed with saturated aqueous solution of $Na_2S_2O_3$ (2×15 ml) and than with H_2O (2×15 ml). The combined organic layers were extracted with EtOAc (2×25 ml), dried (Na_2SO_4), filtered and evaporated under reduced pressure. The residue was purified by column chromatography ($CHCl_3$/MeOH 8:3) to give a yellow solid. Yield 0.65 mg (32%). – M. p. 58 – 62 °C (MeOH). – $[\alpha]_D^{21} = -17.5°$ (*c* 0.5, acetone). – $R_f = 0.35$ ($CHCl_3$/MeOH 8:3). – IR (capillary): $\nu = 3376$ (OH), 2230 (CN) cm^{-1}. – ^{1}H NMR (250 MHz, [D_6]-DMSO): $\delta = 3.33$ (br, 3H, 2'-H, $2 \times$ OH), 3.71 (dd, 1H, 4'a-H), 3.83 (m, 1H, 4'b-H), 4.05 – 4.27 (m, 3H, $J_{2',3'} = 5.8$ Hz, 3'-H, $2 \times$ OH), 4.72 (d, 1H, $J_{1',2'} = 4.57$ Hz, 1'-H), 7.45 – 7.48 (m, 5H, Ph), 7.83 (d, 1H, 6-H), 8.24 (d, 1H, $J_{4,6} = 2.45$ Hz, 4-H). – ^{13}C NMR (62.9 MHz, [D_6]-DMSO) $\delta = 71.4$ (C-4'), 71.6 (C-3'), 72.4 (C-2'), 76.8 (C-1'), 102.9 (C-3), 116.6 (CN), 117.2 (C-5), 126.7 – 129.4 (*o*-, *m*-, *p*-Ph), 143.4 (C-6), 148.6 (C-4), 160.2 (C=O). – MS (CI, *iso*-butane): m/z (%) = 587 (100) (MH^+), 298 (30) $[M]^+ - H_2O$, 225 (100) $[M]^+ - HOCH_2CH(OH)CH(OH)$. – $C_{16}H_{16}N_2O_5$ (316.30): calcd. C 60.75, H 5.10, N 8.86; found C 59.82, H 4.73, N 8.56.

*5-(1,2-Di-O-benzyl-L-arabino-1,2,3-trihydroxy-butyl)-1,2-dihydro-2-oxo-1-phenyl-pyridine-3-carbonitrile (**9**)*

4a (1.0 g, 2.38 mmol) reacted with aniline (0.66 g, 7.14 mmol) as described for the preparation of **7a**. Yield 1.08 g (76%); colorless syrup. – $[\alpha]_D^{22} = +11.0°$ (*c* 0.5, CHCl3). – $R_f = 0.70$ (chloroform/MeOH 9:1). – IR (nujol): $\nu = 3472$ (OH), 2228 (CN), 1666 (C=O) cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 1.18$ (d, 3H, $^3J = 6.5$ Hz, CH_3), 2.36 (d, 1H, $^3J = 5.5$ Hz, OH), 3.23 (dd, 1H, $^3J_{2',1'} = 3.5$ Hz, $^3J_{2',3'} = 6.8$ Hz, 2'-H), 3.88 (m, 1H, 3'-H), 4.29 (d, 1H, $^2J = 11.6$ Hz, C*H*HPh), 4.31 (d, 1H, $^2J = 11.9$ Hz, C*H*HPh), 4.41 (d, 1H, 1'-H), 4.50 (d, 1H, $^2J = 11.9$ Hz, C*H*HPh), 4.61 (d, 1H, $^2J = 11.6$ Hz, C*H*HPh), 7.05 – 7.40 (m, 15H, Ph), 7.44 (d, 1H, $^4J_{4,6} = 2.5$ Hz, 4-H), 7.75 (d, 1H, 6-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta = 20.1$ (CH_3), 67.2 (C-3'), 71.9, 74.3 ($2 \times CH_2$Ph), 76.9 (C-1'), 84.0 (C-2'), 105.9 (C-3), 115.5 (CN), 116.3 (C-5), 126.0 – 129.5 (*o*-, *m*-, *p*-Ph), 136.7, 137.2,

139.5 (3 × *i*-Ph), 141.7 (C-4), 147.2 (C-6), 158.9 (C=O). – MS (CI, *iso*-butane): m/z (%) = 481 (100) (MH^+), 373 (4) ($M\text{-}OCH_2Ph^+$), 315 (10). – $C_{30}H_{28}N_2O_4$ (480.55): calcd. C 74.98, H 5.87, N 5.83; found C 74.70, H 5.58, N 5.65.

*Methyl 2-amino-6-benzyloxymethyl-5-(1,2-di-O-benzyl-D-erythro-1,2,3-trihydroxy-propyl)pyridine-3-carboxylate (**11a**)*

Compound **6a** (0.6 g, 1.14 mmol) was dissolved in EtOH (20 ml). Aqueous ammonia solution (25%, 0.15 ml, 2.28 mmol) was added and the mixture was stirred for 10 min at room temperature. The solvent was evaporated, and the product was purified by flash chromatography (chloroform/ethyl acetate 9:1) and dried *in vacuo*. Yield 0.57 g (92%); colorless syrup. – $[\alpha]_D^{24} = +5.1°$ (*c* 0.8, $CHCl_3$). – $R_f = 0.31$ (chloroform/ethyl acetate 9:1). – IR (capillary): ν = 3460 (OH), 3358 (NH_2), 1692 (C=O), 1616 (NH_2) cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): $\delta = 2.26$ (br, 1H, OH), 3.48 (dt, 1H, $^3J_{2',3'} = 4.5$ Hz, 2'-H), 3.66 (br s, 2H, 3'a-H, 3'b-H), 3.79 (s, 3H, CH_3), 4.12 – 4.35 (5 × d, 5H, $^2J = 11.6$ Hz), 4.47 (center of an AB quartet, 2H, $^2J = 12.0$ Hz), 4.59 (d, 1H, $^2J = 11.6$ Hz), (3 × C*H*$_2$Ph, C*H*$_2$Pyr), 4.72 (d, 1H, $^3J_{1',2'} = 7.6$ Hz, 1'-H), 6.40 (br, 2H, NH_2), 6.85 – 7.30 (m, 15H, Ph), 8.15 (s, 1H, 4-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta = 51.8$ (CH_3), 62.0 (C-3'), 70.7, 71.4, 72.7, 73.1 (*C*H$_2$Pyr, 3 × *C*H$_2$Ph), 76.0 (C-1'), 81.9 (C-2'), 106.1 (C-3), 122.9 (C-5), 127.6 – 128.4 (*o*-, *m*-, *p*-Ph), 137.5, 137.7, 137.9 (3 × *i*-Ph), 140.1 (C-4), 158.1, 160.1 (C-2, C-6), 166.6 (C=O). – MS (CI, *iso*-butane): m/z (%) = 543 (84) (MH^+), 435 (40) ($M\text{-}OCH_2Ph^+$), 391 (48). – $C_{32}H_{34}N_2O_6$ (542.62): calcd. C 70.83, H 6.32, N 5.16. found C 70.39, H 6.39, N 5.07.

*Ethyl 2-amino-6-benzyloxymethyl-5-(1,2-di-O-benzyl-D-erythro-1,2,3-trihydroxy-propyl)pyridine-3-carboxylate (**11b**)*

Compound **6b** (0.6 g, 1.11 mmol) reacted with aqueous ammonia solution (25%, 0.15 ml, 2.28 mmol) as described above for the preparation of **11a**. Yield 0.56 g (90.5%); colorless syrup. – $[\alpha]_D^{21} = +13.7°$ (*c* 1, $CHCl_3$). – $R_f = 0.34$ (chloroform/ethyl acetate 9:1). – IR (capillary): ν = 3454 (OH), 3366 (NH_2), 1694 (C=O), 1611 (NH_2) cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): $\delta = 1.30$ (t, 3H, CH_3), 3.47 (dt, 1H, $^3J_{2',3'} = 4.5$ Hz, 2'-H), 3.68 (m, 2H, 3'a-H, 3'b-H), 4.13 – 4.34 (q, 2H, $^3J = 7.2$ Hz, (C*H*$_2$CH$_3$) and 5 × d, 5H, $^2J = 11.6$ Hz), 4.48 (center of an AB quartet, 2H, $^2J = 12.0$ Hz), 4.61 (d, 1H, $^2J = 11.6$ Hz), (3 × C*H*$_2$Ph, C*H*$_2$Pyr), 4.72 (d, 1H, $^3J_{1',2'} = 7.6$ Hz, 1'-H), 6.38 (s, 2H, NH_2), 6.88 – 7.30 (m, 15H, Ph), 8.15 (s, 1H, 4-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta = 14.3$ (CH_3), 60.9 (*C*H$_2$CH$_3$), 62.1 (C-3'), 70.7, 71.4, 72.7, 73.0 (3 × *C*H$_2$Ph, *C*H$_2$Pyr), 76.0 (C-1'), 81.8 (C-2'), 106.1 (C-3), 122.8 (C-5), 127.6 – 128.4 (*o*-, *m*-, *p*-Ph), 137.5, 137.7, 137.9 (3 × *i*-Ph), 139.9 (C-4), 157.2, 159.6 (C-2, C-6), 166.3 (C=O). – MS (CI, *iso*-butane): m/z (%) = 557 (100) (MH^+), 449 (20) ($M\text{-}OCH_2Ph^+$), 431 (29), 405 (50). – $C_{33}H_{36}N_2O_6$ (556.65): calcd. C 71.20, H 6.52, N 5.03; found C 70.94, H 6.28, N 4.78.

X-ray structure determination of **2b**

The data collection was performed on a Bruker P4 four circle diffractometer with Mo-K$_\alpha$ radiation ($\lambda = 0.71073$ Å) and a graphite monochromator in routine ω-scan after checking the crystal quality by a rotational photo and determining a reasonable reduced cell. Further data: crystal size 0.78 × 0.42 × 0.22 mm^3, $T = 223$ K, $C_{33}H_{33}NO_6$, $M = 539.62$, orthorhombic, space group (H.-M.): $P2_12_12_1$, space group (Hall): *P*2ac 2ab, $a = 939.6$ (10), $b = 1712.4$ (2), $c = 1771.3$ (2) pm, $\alpha = \beta = \gamma = 90°$, $V = 2850 \times 10^6$ pm^3, $Z = 4$, $\rho_{calcd.} = 1.258$ $Mg \cdot m^{-3}$, $\mu = 0.90$ mm^{-1}, $F(000) = 1144$, data collection range: $2.3 \leq \Theta \leq 22.50°$, $-10 \leq h \leq 8$, $-18 \leq k \leq 18$, $-19 \leq l \leq 19$, 4033 reflections collected, 3531 independent reflections, [R(int) = 0.0349], 3065 observed [$I > 2\sigma(I)$], completeness to $\Theta = 22.50°$: 99.5%, $R_1 = 0.0489$ (obs.), $wR_2 = 0.1199$ (obs.), $R_1 = 0.0599$ (all), $wR_2 = 0.1293$ (obs.), GOF (F^2) = 1.058, max./min. residual electron density: $+0.22/-0.18$ e· $Å^{-3}$. The weighting scheme was calculated according to $w^{-1} = \sigma^2(F_o^2) + (0.0557P)^2 + 0.7163P$ with $P = (F_o^2 + 2F_c^2)/3$.

The structure was solved by direct methods (SHELXS-86, G.M. Sheldrick, Universität Göttingen, 1986) and refined by the full matrix least-squares method of the Bruker SHELXTL software package. All non-hydrogen atoms were refined anisotropically with the hydrogen atoms introduced into theoretical positions and refined according to the riding model.

CCDC-145504 contains the supplementary crystallographic data for this compound. 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.

X-ray structure determination of **4b**

Crystal size 0.30 × 0.26 × 0.58 mm^3, $T = 293$ K, $C_{26}H_{27}NO_5$, $M = 433.50$, orthorhombic, space group (H.-M.): $P2_12_12_1$, space group (Hall): *P*2ac 2ab, $a = 1036.8$ (1), $b = 1506.3$ (3), $c = 1542.6$ (2) pm, $\alpha = \beta = \gamma = 90°$, $V = 2409 \times 10^6$ pm^3, $Z = 4$, $\rho_{calcd.} = 1.195$ $Mg \cdot m^{-3}$, $\mu = 0.83$ mm^{-1}, $F(000) = 920$, data collection range: $1.89 \leq \Theta \leq 22.00°$, $-10 \leq h \leq 10$, $-15 \leq k \leq 15$, $-16 \leq l \leq 16$, 3411 reflections collected, 2954 independent reflections, [R(int) = 0.0348], 1871 observed [$I > 2\sigma(I)$], completeness to $\Theta = 22.00°$: 100% $R_1 = 0.0618$ (obs.), $wR_2 = 0.1317$ (obs.), GOF (F^2) = 0.999, max./min. residual electron density: $+0.14/-0.14$ e· $Å^{-3}$. The weighting scheme was calculated

according to $w^{-1} = \sigma^2(F_o^2) + (0.0560P)^2 + 0.000P$ with $P = (F_o^2 + 2F_c^2)/3$.

CCDC-145505 contains the supplementary crystallographic data for this compound.

Acknowledgements

We thank the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for financial support.

[1] W. Priebe, G. Grynkiewicz, N. Neamati, Tetrahedron Lett. **33**, 7681 (1992).
[2] M. Jung, S. W. Tinachoe, Tetrahedron Lett. **34**, 6247 (1993).
[3] C. Lamberth, M. Bednarski, Carbohydrate Lett. 369 (1995).
[4] M. Hayashi, K. Tsukada, H. Kawabata, C. Lamberth, Tetrahedron **55**, 12287 (1999).
[5] N. G. Ramesh, K. K. Balasubramanian, Tetrahedron Lett. **32**, 3875 (1991).
[6] I. Rudloff, K. Peseke, H. Reinke, J. Prakt. Chem. **340**, 334 (1998).
[7] K. Peseke, Z. Chem. **17**, 288 (1977).
[8] M. Michalik, K. Peseke, R. Radeglia, J. Prakt. Chem. **323**, 506 (1981).
[9] K. Peseke, J. Prakt. Chem. **323**, 499 (1981).
[10] D. Michalik, H. Feist, K. Peseke, Carbohydr. Res. **333**, 197 (2001).
[11] K. Peseke, S. Aldinger, H. Reinke, Liebigs Ann. 953 (1996).
[12] I. Rudloff, M. Michalik, A. Montero, K. Peseke, Synthesis 1686 (2001).
[13] A. Montero, H. Feist, M. Michalik, J. Quincoces, K. Peseke, Synthesis 664 (2002).
[14] A. Montero, H. Feist, M. Michalik, J. Quincoces, K. Peseke, J. Carbohydr. Chem. **21**, 305 (2002).
[15] L. L. Shen, S. K. Tanaka, D. T. W. Chu, Current Pharmaceutical Design. **3**, 169 (1997).
[16] M. H. Paluchowska, R. Bugno, S. Charakchieva-Minol, A. J. Bojarski, A. Wesołowska, Pol. J. Pharmacol. **53**, 369 (2001).
[17] E. Bisagny, V. Dolle, M. Nguyen, M. Legraverend, A. M. Aubertin, A. Kirn, M. L. Andreola, L. Tarrago-Litvak, M. Ventura, French Patent, 95 09323, December 19, 1997.
[18] M. Hesse, H. Meier, B. Zeeh, Spektroskopische Methoden in der organischen Chemie, p. 139, Georg Thieme Verlag, Stuttgart (1987).
[19] H. Friebolin, Ein- und zweidimensionale NMR-Spektroskopie, p. 83, Wiley-VCH Verlag, Weinheim (1988).
[20] K. Peseke, H. Feist, W. Hanefeld, J. Kopf, H. Schulz, J. Carbohydr. Chem. **14**, 317 (1995).
[21] D. Bouvy, Z. Janousek, H. G. Viehe, B. Tinant, J. P. Declerq, Tetrahedron Lett. **34**, 1779 (1993).
[22] F. Nicotra, R. Perego, F. Ronchtetti, G. Russo, L. Toma, Carbohydr. Res. **131**, 180 (1984).
[23] M. E. Jung, M. A. Lyster, J. Org. Chem. **42**, 3761 (1977).