Synthesis of a 2′-(Acetamido)fucobioside

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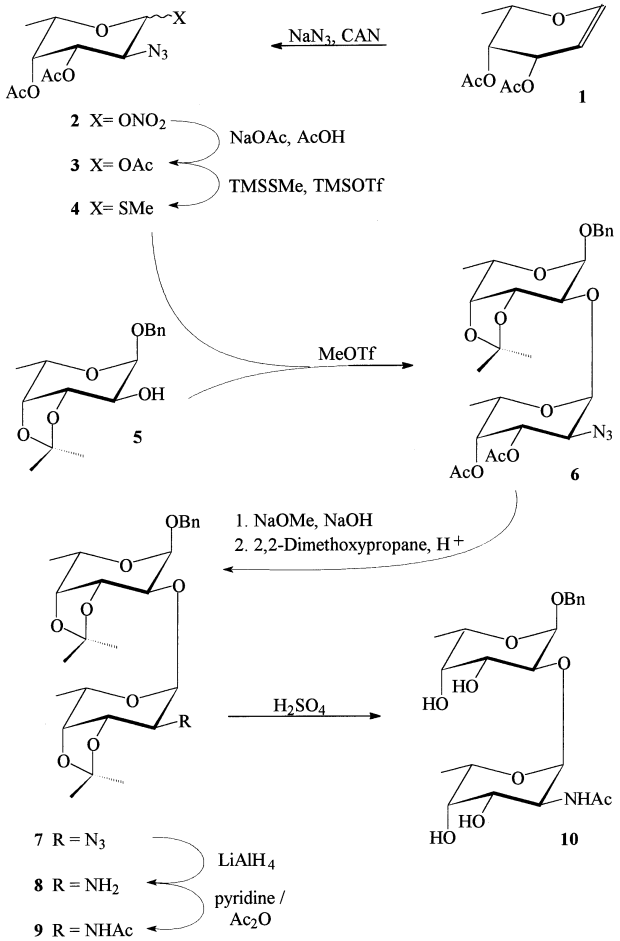
The 2-azidofucosyl donor **4** was synthesised via a azidonitratisation and stereoselectively α-linked to the benzyl fucoside acceptor **5** by methyl triflate catalysis. The resulting disaccharide **6** could be transformed to the corresponding acetamido derivative and deprotected to 2′-(acetamido)fucobioside **10**

Since lung-specific lectins are identified as the responsible factor for the adhesion of disseminated tumor cells,[1] we have investigated several aspects of enhancing the blocking capacity of fucose by employing approaches such as oligomerisation,[2] clustering[3] and derivatisation.[4] This paper reports the preparation of a thiomethyl 2-azidofucosyl donor and its application to the synthesis of 2-amino- and 2-acetamido-α-fucopyranose containing disaccharides.

Aminosugars such as *N*-acetylglucosamine, *N*-acetylneuraminic acid and *N*-acetylgalactosamine are widely spread in nature and belong to the group of sugars that are often required by the metabolism of higher organisms. Other glycosamines are rather seldom, often carry the amino group at a different position and occur mainly in plants and bacteria. They are known to act as potent inhibitors of enzymes and are sometimes part of antibiotic or other biologically active glycosides. Fucosamines are found in microorganisms as well,[5][6] were isolated from them[7] and synthesised chemically.[8] By providing an easy and selective method for the synthesis of 2-amino-fucosides their potential in lectin inhibition can be investigated.

Starting from 3,4-di-*O*-acetyl-1,5-anhydro-2,6-dideoxy-L-lyxo-hex-1-enitol (3,4-di-*O*-acetyl-L-fucal, **1**),[9] the azido group was introduced employing the azidonitratisation method of Lemieux et al.[10] The resulting anomeric mixture of nitrates **2** was not isolated but directly converted into the corresponding acetates **3** by heating the crude product with acetic acid and sodium acetate. Chromatography gave 51% of the anomeric mixture **3**, and no trace of the *talo*-configured epimer could be detected. The conversion into the thioglycoside was performed with trimethylsilyl methylsulfide (TMSSMe) and trimethylsilyl triflate (TMSOTf) in nearly quantitative yields to give the product **4** as an anomeric mixture.

Attempts to activate the thioglycoside with halonium ions met with problems. The use of *N*-iodosuccinimide (NIS) as well as $CuBr_2/Bu_4NBr$ together with a glycosyl acceptor did not lead to the formation of a new glycoside; the latter did not even form the corresponding bromide precursor but in both cases starting materials could be recovered quantitatively. However, the use of methyl triflate together with the acceptor molecule **5** proved to be a successful activation method and stereoselectively led to the disaccharide **6** in a 73% yield without any *O*-methylation of the acceptor. Following deacetylation and isopropylidenation to **7** the reduction could be performed with lithium alu-



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minium hydride. By acetylation of the amine **8** with pyridine/acetanhydride and acid de-isopropylidenation of **9** the target compound 2-acetamido fucobioside **10** could be obtained and characterised. No traces of hydrolysis products of **9** or **10** could be detected.

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Experimental Section

General: NMR spectra were recorded with a Bruker AMX-400 spectrometer, reference TMS. Some assignments were made with support of $^1H^1H$- and $^1H^{13}C$-COSY experiments. *Ambiguous assignment of protons is denoted with an asterisk* (*). Optical rotation were measured with a Perkin-Elmer polarimeter 243. TLC was performed on silica gel coated foil (silica gel 60 F_{254} Merck, Darmstadt). Preparative column chromatography was performed with silica gel 60 (63−200μm, Merck, Darmstadt).

1,3,4-Tri-O-acetyl-2-azido-2-deoxy-L-fucopyranose (**3**): A solution of diacetyl-L-fucal (**1**, 1.66 g, 7.75 mmol) in anhydrous acetonitrile (70 ml) was dropped to sodium azide (0.76 g, 11.7 mmol) and cerammonium nitrate (CAN, 12.75 g, 23.25 mmol)) at −15°C and stirred for a night under argon. The solution was diluted with ether (100 ml), washed four times with water, dried with magnesium sulfate, filtered and the solvent removed. The remaining solids were taken up in acetic acid (50 ml), with a catalytic amount of acetic anhydride, and sodium acetate (3.0 g) were added and the mixture was refluxed for 2 h. The solution was poured into ice water and extracted four times with dichloromethane. The organic layer was subsequently washed three times with satd. sodium hydrogen carbonate solution and once with satd. sodium chloride solution, dried with magnesium sulfate, filtered, the solvent removed and evaporated three times with toluene. Column chromatography (petroleum ether/ethyl acetate, 3:1) yielded 1.25 g (3.96 mmol, 51%, α/β 5:4) product as an anomeric mixture. − ^1H NMR (400 MHz, $CDCl_3$): δ = 1.15 (d, $J_{5,6}$ = 6.6 Hz, 3 H, H-6α), 1.21 (d, $J_{5,6}$ = 6.6 Hz, 3 H, H-6β), 2.06 (s, 3 H, OAc), 2.08 (s, 3 H, OAc), 2.16 (s, 3 H, OAc), 2.18 (s, 3 H, OAc), 2.19 (s, 3 H, OAc), 2.20 (s, 3 H, OAc), 3.81 (dd, $J_{1,2}$ = 8.6 Hz, $J_{2,3}$ = 10.7 Hz, 1 H, H-2β), 3.90 (dd ≈ m, 1 H, H-2α), 3.91 (dq ≈ m, $J_{4,5}$ = 1.0 Hz, $J_{5,6}$ = 6.6 Hz, 1 H, H-5β), 4.20 (dq, $J_{4,5}$ = 1.0 Hz, $J_{5,6}$ = 6.6 Hz, 1 H, H-5α), 4.89 (dd, $J_{2,3}$ = 10.7 Hz, $J_{3,4}$ = 3.5 Hz, 1 H, H-3β), 5.23 (dd, $J_{3,4}$ = 3.5 Hz, $J_{4,5}$ = 1.0 Hz, 1 H, H-4β), 5.33 (dd ≈ m, 1 H, $J_{3,4}$ = 3.0 Hz, $J_{4,5}$ = 1.0 Hz, H-4α), 5.33 (dd ≈ m, $J_{3,4}$ = 3.0 Hz, 1 H, H-3α), 5.53 (d, $J_{1,2}$ = 8.6 Hz, 1 H, H-1β), 6.29 (d, $J_{1,2}$ = 3.6 Hz, 1 H, H-1α).

Methyl 3,4-Di-O-acetyl-2-azido-2-deoxy-1-thio-L-fucopyranoside (**4**): Compound **3** (1021 mg, 3.24 mmol) was evaporated with toluene three times and subsequently dissolved in anhydrous dichloromethane (25 ml) under argon. The solution was chilled to 0°C and TMSSMe (0.96 ml, 6.75 mmol) followed by TMSOTf (1.0 ml, 5.51 mmol) were slowly added. The mixture was allowed to warm to room temperature with stirring for about 10 h. For workup the solution was washed three times with satd. sodium hydrogen carbonate solution and once with sodium chloride solution, dried with magnesium sulfate, filtered and the solvent removed. Column chromatography (petroleum ether/ethyl acetate, 3:1) gave 866 mg (2.85 mmol, 88%, α/β 2:1) product as colourless syrup. − ^1H-NMR (400 MHz, $CDCl_3$): δ = 1.17 (d, $J_{5,6}$ = 6.6 Hz, 3 H, H-6α), 1.22 (d, $J_{5,6}$ = 6.6 Hz, 3 H, H-6β), 2.04 (s, 3 H, OAcα), 2.06 (s, 3 H, OAcβ), 2.12 (s, 3 H, OAcα), 2.17 (s, 3 H, OAcβ), 2.18 (s, 3 H, SMeα), 2.28 (s, 3 H, SMeβ), 3.69 (dd ≈ t, $J_{1,2}$ = $J_{2,3}$ = 10.2 Hz, 1 H, H-2β), 3.78 (dq, $J_{4,5}$ = 1.0 Hz, $J_{5,6}$ = 6.6 Hz, 1 H, H-5β), 3.90 (dd, $J_{1,2}$ = 5.6 Hz, $J_{2,3}$ = 11.2 Hz, 1 H, H-2α), 4.28 (d, $J_{1,2}$ = 10.2 Hz, 1 H, H-1β), 4.44 (dq, $J_{4,5}$ = 1.0 Hz, $J_{5,6}$ = 6.6 Hz, 1 H, H-5α), 4.89 (dd, $J_{2,3}$ = 10.2 Hz, $J_{3,4}$ = 3.5 Hz, 1 H, H-3β), 5.15 (dd, $J_{2,3}$ = 11.2 Hz, $J_{3,4}$ = 3.6 Hz, 1 H, H-3α), 5.24 (dd, $J_{3,4}$ = 3.5 Hz, $J_{4,5}$ = 1.0 Hz, 1 H, H-4β), 5.28 (dd, $J_{3,4}$ = 3.6 Hz $J_{4,5}$ = 1.0 Hz, 1 H, H-4α), 5.34 (d, $J_{1,2}$ = 5.6 Hz, 1 H, H-1α) . − $C_{11}H_{17}O_5N_3S$ (303.34): calcd. C 43.56, H 5.65, N 13.85; found C 43.82, H 5.66, N 13.19.

Benzyl 3,4-Di-O-acetyl-2-azido-2-deoxy-α-L-fucopyranosyl-(1→2)-3,4-O-isopropylidene-α-L-fucopyranoside (**6**): Donor **4** (100 mg, 0.33 mmol and acceptor **5** (150 mg, 0.51 mmol) were evaporated twice with toluene and subsequently stirred in anhydrous dichloromethane (10 ml) with freshly activated molecular sieves (4 Å) for 1 h. Then methyl triflate (65 μl, 1.5 mmol) was added and the mixture was stirred over night. For workup triethylamine (0.5 ml) was added, after 1 h the suspension diluted with dichloromethane, washed three times with satd. sodium hydrogen carbonate solution and once with satd. sodium chloride solution, dried with magnesium sulfate, filtered and the solvent removed. After column chromatography (petroleum ether/ethyl acetate 7:2) 132 mg (0.24 mmol, 73%) of the anomerically pure disaccharide remained. − $[\alpha]^{20}_D$ = −183.4 (*c* = 1.0, $CHCl_3$). − IR ($CHCl_3$, λ^{-1}): 2110 cm^{-1} (N_3). − ^1H-NMR (400 MHz, $CDCl_3$): δ = 1.10 (d, $J_{5,6}$ = 6.6 Hz, 3 H, H-6*), 1.34 (d, $J_{5,6}$ = 6.6 Hz, 3 H, H-6*), 1.35 (s, 3 H, ^{i}Pr), 1.50 (s, 3 H, ^{i}Pr), 2.05 (s, 3 H, OAc), 2.15 (s, 3 H, OAc), 3.59 (dd, $J_{1',2'}$ = 3.6 Hz, $J_{2',3'}$ = 11.2 Hz, 1 H, H-2′), 3.80 (dd, $J_{1,2}$ = 3.6 Hz, $J_{2,3}$ = 8.1 Hz, 1 H, H-2), 4.06 (dd, $J_{3,4}$ = 5.6 Hz, $J_{4,5}$ = 2.5 Hz, 1 H, H-4), 4.14 (dq, $J_{4,5}$ = 2.5 Hz, $J_{5,6}$ = 6.6 Hz, 1 H, H-5), 4.31 (dd, $J_{2,3}$ = 8.1 Hz, $J_{3,4}$ = 5.6 Hz, 1 H, H-3), 4.46 (dq, $J_{4',5'}$ = 1.0 Hz, $J_{5',6'}$ = 6.6 Hz, 1 H, H-5′), 4.58 (d, *J* = 11.7 Hz, 1 H, CH_2Ph), 4.72 (d, *J* = 11.7 Hz, 1 H, CH_2Ph), 4.92 (d, $J_{1,2}$ = 3.5 Hz, 1 H, H-1*), 4.95 (d, $J_{1,2}$ = 3.5 Hz, 1 H, H-1*), 5.31 (dd, $J_{3',4'}$ = 3.6 Hz, $J_{4',5'}$ = 1.0 Hz, 1 H, H-4′), 5.45 (dd, $J_{2',3'}$ = 11.2 Hz, $J_{3',4'}$ = 3.6 Hz, 1 H, H-3′), 7.34 (m, 5 H, aryl-H) . − ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 15.76 (C-6*),16.27 (C-6*), 20.64 and 20.71 (2 × CO*C*H_3), 26.38 and 28.50 [C(*C*H_3)$_2$], 69.63 (*C*H_2Ph), 57.22, 63.33, 64.69, 68.58, 70.84, 74.20, 74.46, 76.13 (2 × C-2, 2 × C-3, 2 × C-4, 2 × C-5), 94.39 (C-1*), 95.61 (C-1*), 108.79 [*C*(CH$_3$)$_2$], 127.95, 128.32, 128.38 and 136.92 (aryl-C), 169.73 and 170.42 (2 × *C*OCH$_3$) . − $C_{26}H_{35}O_{10}N_3$ (549.58): calcd. C 56.82, H 6.42, N 7.65; found C 57.00, H 6.60, N 7.13.

Benzyl 2-Azido-2-deoxy-3,4-O-isopropylidene-α-L-fucopyranosyl-(1→2)-3,4-O-isopropylidene-α-L-fucopyranoside (**7**): Compound **6** (98 mg, 0.18 mmol) was dissolved in methanol (50 ml) and stirred over night with a catalytic amount of sodium methanolate. The solution was neutralised by stirring with ion exchange resin (Amberlite IR-120, H^+) and the solvent removed under reduced pressure. The amorphous white residue was subsequently dissolved in dichloromethane (50 ml) and isopropylidenated with 2,2-dimethoxypropane (2.0 ml) for 2 h. For workup the solution was washed three times with satd. sodium hydrogencarbonate solution and once with sodium chloride solution, dried with magnesium sulfate and filtered. After removing the solvent 82 mg (0.16 mmol, 89%) disaccharide were isolated. − $[\alpha]^{20}_D$ = −332.1 (*c* = 1.0, $CHCl_3$). − ^1H-NMR (400 MHz, $CDCl_3$): δ = 1.30 (d, $J_{5,6}$ = 6.6 Hz, 3 H, H-6*), 1.33 (d, $J_{5,6}$ = 6.6 Hz, 3 H, H-6*), 1.34 (s, 3 H, ^{i}Pr), 1.36 (s, 3 H, ^{i}Pr), 1.51 (s, 3 H, ^{i}Pr), 1.52 (s, 3 H, ^{i}Pr), 3.29 (dd, $J_{1',2'}$ = 3.6 Hz, $J_{2',3'}$ = 8.6 Hz, 1 H, H-2′), 3.78 (dd, $J_{1,2}$ = 3.6 Hz, $J_{2,3}$ = 8.1 Hz, 1 H, H-2), 4.04 (dd, $J_{3,4}$ = 5.1 Hz, $J_{4,5}$ = 2.5 Hz, 1 H, H-4*), 4.10 (dd, $J_{3,4}$ = 5.1 Hz, $J_{4,5}$ = 2.5 Hz, 1 H, H-4*), 4.13 (dq, $J_{4,5}$ = 2.5 Hz, $J_{5,6}$ = 6.6 Hz, 1 H, H-5*), 4.27 (dd, $J_{2,3}$ = 8.1 Hz, $J_{3,4}$ = 5.1 Hz, 1 H, H-3), 4.43 (dd, $J_{2',3'}$ = 8.6 Hz, $J_{3',4'}$ = 5.1 Hz, 1 H, H-3′), 4.51 (dq, $J_{4,5}$ = 2.5 Hz, $J_{5,6}$ = 6.6 Hz, 1 H, H-5*), 4.58 (d, *J* =

11.7 Hz, 1 H, CH_2Ph), 4.71 (d, J = 11.7 Hz, 1 H, CH_2Ph), 4.78 (d, $J_{1,2}$ = 3.6 Hz, 1 H, H-1*), 4.95 (d, $J_{1,2}$ = 3.6 Hz, 1 H, H-1*), 7.35 (m, 5 H, aryl-H). − ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 16.10 (C-6*), 16.27 (C-6*), 26.35, 26.46, 28.40 and 28.48 [4 × C(CH_3)$_2$], 61.08, 63.05, 63.28 (C-2′, 2 × C-5), 69.66 (CH_2Ph), 73.31, 73.73, 74.54, 75.66, 76.22 (C-2, 2 × C-3, 2 × C-4), 94.30 (C-1*), 95.14 (C-1*), 108.78 and 109.24 [2 × C(CH_3)$_2$], 127.98, 128.36, 128.39 and 136.90 (aryl-C) .

Benzyl 2-Acetamido-2-deoxy-3,4-O-isopropylidene-α-L-fucopyranosyl-(1→2)-3,4-O-isopropylidene-α-L-fucopyranoside (**9**): The azide **7** (80 mg, 0.158 mmol) was dissolved in anhydrous THF (10 ml) under argon and treated with lithium aluminium hydride (50 mg) at 20°C for 1 h. The excess of $LiAlH_4$ was destroyed with methanol (1 ml), then water (30 ml) was added and the mixture was extracted twice with dichloromethane. The organic layer was washed twice with satd. sodium chloride solution, dried with magnesium sulfate, filtered and the solvent removed. The residue **8** was first evaporated with toluene and then acetylated over night, using pyridine/acetanhydride (15 ml). The solvent was removed and the residue evaporated with toluene four times furnishing 79 mg (0.152 mmol, 96%) product as amorphous solid. − $[\alpha]^{20}_D$ = −446.2 (c = 2.0, $CHCl_3$). − IR ($CHCl_3$, λ^{-1}): 1662 cm^{-1} (amide I), 1543 cm^{-1} (amide II). − ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.34 (m, 9 H, ^{i}Pr, 2 × H-6), 1.36 (s, 3 H, ^{i}Pr), 1.52 (s, 3 H, ^{i}Pr), 1.58 (s, 3 H, ^{i}Pr), 1.73 (s, 3 H, NHAc), 3.82 (dd, $J_{1,2}$ = 3.6 Hz, $J_{2,3}$ = 8.1 Hz, 1 H, H-2), 4.06 (m, 3 H, H-3*, 2 × H-4), 4.10 (dq, $J_{4,5}$ = 2.5 Hz, $J_{5,6}$ = 6.6 Hz, 1 H, H-5*), 4.23 (dd ≈ m, $J_{2,3}$ = 8.1 Hz, $J_{3,4}$ = 5.6 Hz, 1 H, H-3), 4.24 (ddd ≈ m, $J_{1',2'}$ = 3.6 Hz, 1 H, H-2′), 4.44 (d, J = 11.7 Hz, 1 H, CH_2Ph), 4.48 (dq, $J_{4,5}$ = 2.5 Hz, $J_{5,6}$ = 6.6 Hz, 1 H, H-5*), 4.76 (d, J = 11.7 Hz, 1 H, CH_2Ph), 4.77 (d, $J_{1,2}$ = 3.6 Hz, 1 H, H-1*), 4.94 (d, $J_{1,2}$ = 3.6 Hz, 1 H, H-1*), 5.59 (d, $J_{2',NH}$ = 9.7 Hz, 1 H, NH), 7.33 (m, 5 H, aryl-H) . − ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 16.28 (C-6*), 16.30 (C-6*), 23.12 (NHCOCH_3), 26.43, 26.61, 28.01 and 28.30 [4 × C(CH_3)$_2$], 50.03 (C-2′), 62.97, 63.47 (2 × C-5), 69.87 (CH_2Ph), 73.06, 74.45, 74.76, 75.46, 76.13 (C-2, 2 × C-3, 2 × C-4), 95.20 (C-1*), 95.42 (C-1*), 108.99 and 109.22 [2 × C(CH_3)$_2$], 127.24, 128.08, 128.65 and 137.21 (aryl-C), 169.89 (NHCOCH$_3$) . − $C_{27}H_{39}O_9N$ (521.61): calcd. C 62.17, H 7.54, N 2.69, found C 62.54, H 7.33, N 2.98.

Benzyl 2-Acetamido-2-deoxy-α-L-fucopyranosyl-(1→2)-α-L-fucopyranoside (**10**): **9** (40 mg, 0.076 mmol) was treated with dioxane/1% aq. sulphuric acid (1:1, 1.0 ml) and stirred at 20°C for 1 d. Neutralisation was done with barium carbonate and the mixture stirred for 1 h. After filtration the solvent was removed under reduced pressure to furnish 32 mg (0.072 mmol, 97%) of a colourless solid. − M.p. 246−249°C. − $[\alpha]^{20}_D$ = −97.3 (c = 0.5, DMSO). − ^{1}H-NMR (400 MHz, DMSO): δ = 1.06 (d, $J_{5,6}$ = 6.6 Hz, 3 H, H-6*), 1.07 (d, $J_{5,6}$ = 6.6 Hz, 3 H, H-6*), 1.66 (s, 3 H, NHAc), 3.48 (dd ≈ d, $J_{3',4'}$ = 3.5 Hz, $J_{4',5'}$ < 1 Hz, 1 H, H-4′), 3.53 (dd ≈ d, $J_{3,4}$ = 3.5 Hz, $J_{4,5}$ < 1 Hz, 1 H, H-4), 3.70 (dd ≈ m, $J_{1,2}$ = 3.6 Hz, 1 H, H-2), 3.72 (m, 2 H, 2 × H-3), 3.80 (dq ≈ q, $J_{4,5}$ < 1 Hz, $J_{5,6}$ = 6.6 Hz, 1 H, H-5), 3.96 (ddd ≈ m, $J_{1',2'}$ = 3.6 Hz, 1 H, H-2′), 4.10 (dq ≈ q, $J_{4',5'}$ < 1 Hz, $J_{5',6'}$ = 6.6 Hz, 1 H, H-5′), 4.40 (d, J = 12.2 Hz, 1 H, CH_2Ph), 4.59 (d, J = 12.2 Hz, 1 H, CH_2Ph), 4.80 (d, $J_{1',2'}$ = 3.6 Hz, 1 H, H-1′), 4.89 (d, $J_{1,2}$ = 3.6 Hz, 1 H, H-1), 7.06 (d, $J_{2',NH}$ = 8.2 Hz, 1 H, NH), 7.33 (m, 5 H, aryl-H) . − ^{13}C-NMR (100 MHz, DMSO): δ = 16.51 (C-6*), 16.79 (C-6*), 22.89 (NHCOCH_3), 49.91 (C2′), 68.80 (CH_2Ph), 66.09, 66.23, 67.57, 68.06, 71.19, 71.67 (C-2, 2 × C-3, 2 × C-4, 2 × C-5), 94.29 (C-1*), 95.44 (C-1*), 127.48, 128.35 and 138.33 (aryl-C), 169.58 (NHCOCH$_3$) .

[1] C. Kieda, M. Monsigny, *Invasion Metastasis* **1986**, *6*, 347−366.
[2] M. Ludewig, J. Thiem, *Synthesis* **1998**, 56−62.
[3] T. K. Lindhorst, M. Ludewig, J. Thiem, *J. Carbohydr. Chem.* **1998**, *17*, in press.
[4] M. Ludewig, D. Lazarevic, J. Kopf, J. Thiem, *J. Chem. Soc., Perkin Trans. 1*, in press.
[5] G. T. Barry, E. Roark, *Nature (London)* **1964**, *202*, 493−494.
[6] S. A. Barker, J. S. Brimacombe, M. J. How, M. Stacey, J. M. Williams, *Nature (London)* **1961**, *189*, 303−304.
[7] J. A. Cifonelli, P. A. Rebers, M. B. Perry, J. K. N. Jones, *Biochemistry* **1966**, *5*, 3066−3072.
[8] A. K. M. Anisuzzaman, D. Horton, *Carbohydr. Res.* **1987** **169**, 258−262.
[9] L. Somsák, I. Németh, *J. Carbohydr. Chem.* **1993**, *12*, 679−684.
[10] R. U. Lemieux, R. M. Ratcliffe, *Can. J. Chem.* **1979**, *57*, 1244−1251.

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