Pergamon

Tetrahedron, Vol. 53, No. 5, pp. 1665-1674, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(96)01114-3

Search for New Moenomycin Structure-Activity Relationships
Synthesis of a Trisaccharide Precursor of a Moenomycin Analogue

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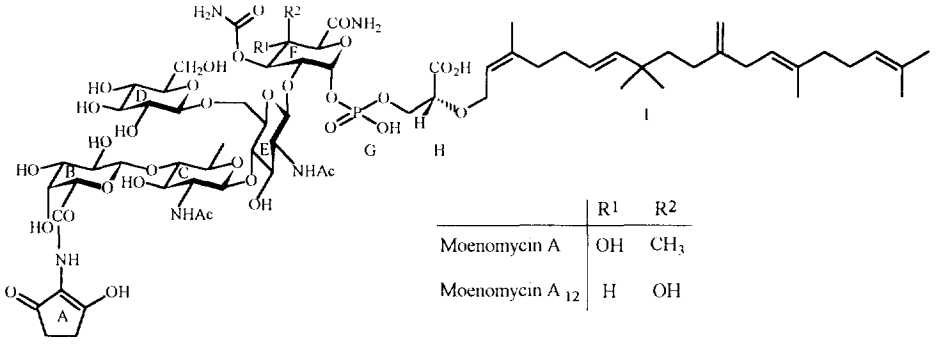
Abstract - On the way to a trisaccharide analogue of the antibiotic moenomycin A a trisaccharide intermediate has been prepared making use of a combination of Danishefsky's sulfonamidoglycosylation and the Schmidt trichloroacetimidate procedure.

Introduction

Two characteristic members of the moenomycin family of antibiotics are the moenomycins A^1 and $A_{12}{}^2$ (see Figure 1). Structurally, they differ only marginally from each other. Whereas in moenomycin A unit F is derived from 4-C-methyl-D-glucuronic acid, in moenomycin A_{12} the branching methyl group is lacking and unit F has D-*galacto* configuration.

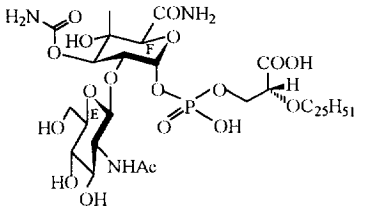


	R1	R2
Moenomycin A	OH	CH_3
Moenomycin A_{12}	H	OH

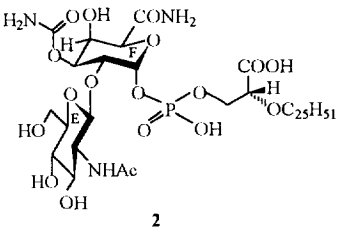
Figure 1. Structures of moenomycins A and A_{12}

This seemingly simple difference has, however, important consequences in terms of structure-activity-relationships. The smallest degradation product of moenomycin A that retains full antibiotic activity is the disaccharide

analogue **1**.[3] In contrast, the smallest antibiotically active degradation product of moenomycin A_{12} is the tri saccharide derivative **3a** whereas **2** is inactive.[2] This result has been confirmed with synthetic compounds (**3b**[4] and **2**[5]).



1



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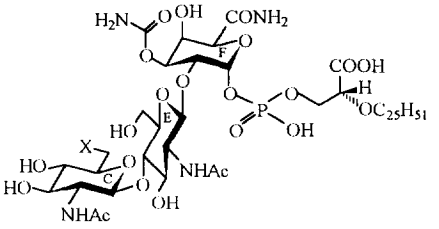
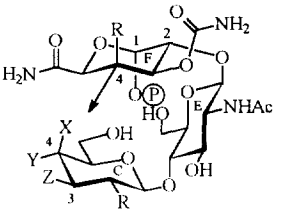


3	X
a	H
b	OH



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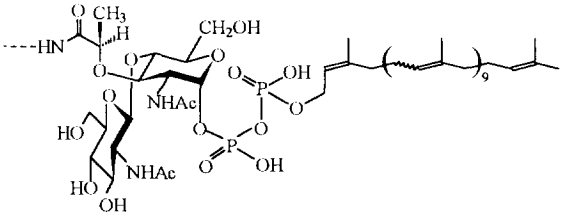

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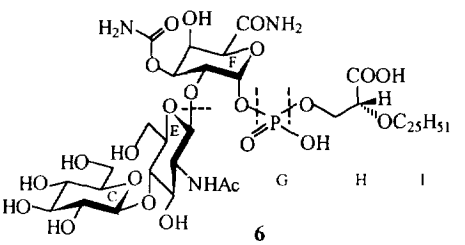
The moenomycins and structural analogues derived therefrom have been shown to specifically inhibit the transglycosylation reaction, one of the final steps in the biosynthesis of bacterial peptidoglycan.[6] Based on experimental work, they are assumed to compete with the immediate peptidoglycan membrane-bound precursor **5**

(lipid II) for the binding site at the enzyme, most probably as a result of structural similarities.[3] The conformations of **1** in solution and after binding to the enzyme are unknown because of experimental difficulties. Moenomycin and its structural analogues are amphiphilic compounds that form aggregates in aqueous solution resulting in broad-line ^{1}H NMR spectra.[7] As a working model we have used a bent conformation for both **1** and lipid II (**5**). The structural similarities of these conformations are immediately evident. Why now is **1** active and the structurally closely related **2** is not? Leaving the methyl group for the moment aside, the only difference between **1** and **2** is the configuration at C-4 of unit F. One may conclude that the equatorial 4^F-OH group is a prerequisite of antibiotic activity in disaccharide analogues and that this OH group is involved in a hydrogen bond to the binding site of the enzyme. Since lipid II (**5**), the real substrate for the enzyme, carries an OR group (R≠H) at the corresponding position this oxygen function is most likely acting as a hydrogen bond acceptor.

At present it is not clear whether there is but a single binding site for moenomycin-type transglycosylase inhibitors at the enzyme. If so, the function of the third sugar (C) in the active trisaccharides **3a** and **3b** might be to mimic the equatorial OH group at C-4 in unit F of **1** as a hydrogen bond acceptor. This is seen in conformation **4** which is derived from **3b** by proper alignment of ring C. In conformation **4** either an equatorial OH group at C-3 (Z) or an axial OH group at C-4 (X) could serve as the hydrogen bond acceptor in place of the equatorial 4-OH group in unit F (see arrow in formula **4**).



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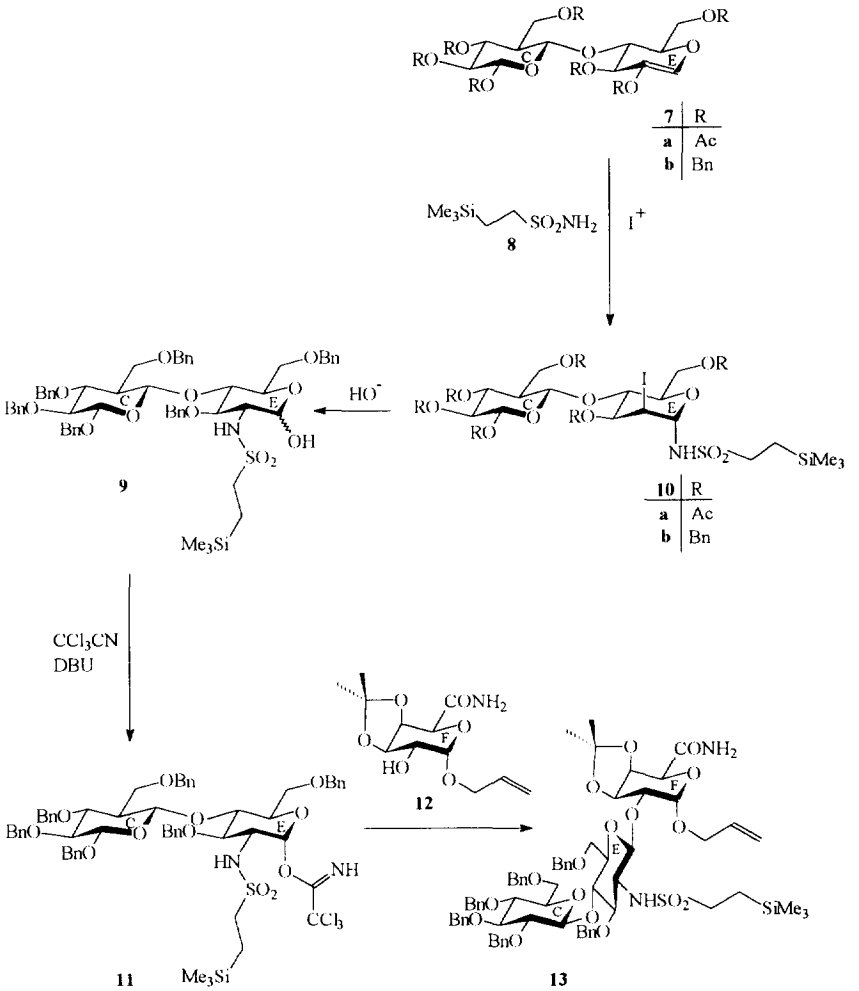
It is the purpose of the present and the accompanying papers to probe this speculation by experiment. We describe the synthesis and antibiotic properties of compound **6** which differs from **3b** by the replacement NHAc→OH at position 2 of ring C. In addition, synthesis of a type **4** compound with D-*galacto* configuration in ring C is reported in the third paper of this series. If the above considerations were correct the NHAc group in ring C of type **3** trisaccharide analogues should be of little influence as far as transglycosylase inhibition is concerned, i.e. **6** and its ring C D-*galacto* stereoisomer should be active.

Synthetic planning for 6 and synthesis of trisaccharide intermediate 12

The retrosynthetic analysis as indicated in formula **6** leads to three precursors: a C-E-F trisaccharide, a phosphoric acid equivalent G, and an equivalent of H-I, which can be obtained from moenomycin by degradation.[8] For the synthesis of C-E-F a two-step approach was envisioned: (i) to use Danishefsky's sulfonamidoglycosylation procedure[9,10] for the preparation of a disaccharide equivalent of C-E and (ii) to couple C-E to unit F. From this analysis a derivative of cellobial as starting material for the synthesis is derived.



Octaacetylcellobiose was converted into the 1-bromo derivative[11] which in turn was reduced with zinc in acetic acid to provide **7a**[12] (hexaacetylcellobial). **7a** was treated with 2-(trimethylsilyl)ethanesulfonamide (**8**)[13,10] in the presence of iodonium-di-sym-collidine perchlorate (IDCP)[14] to provide sulfonamide **10a** in 58% yield.

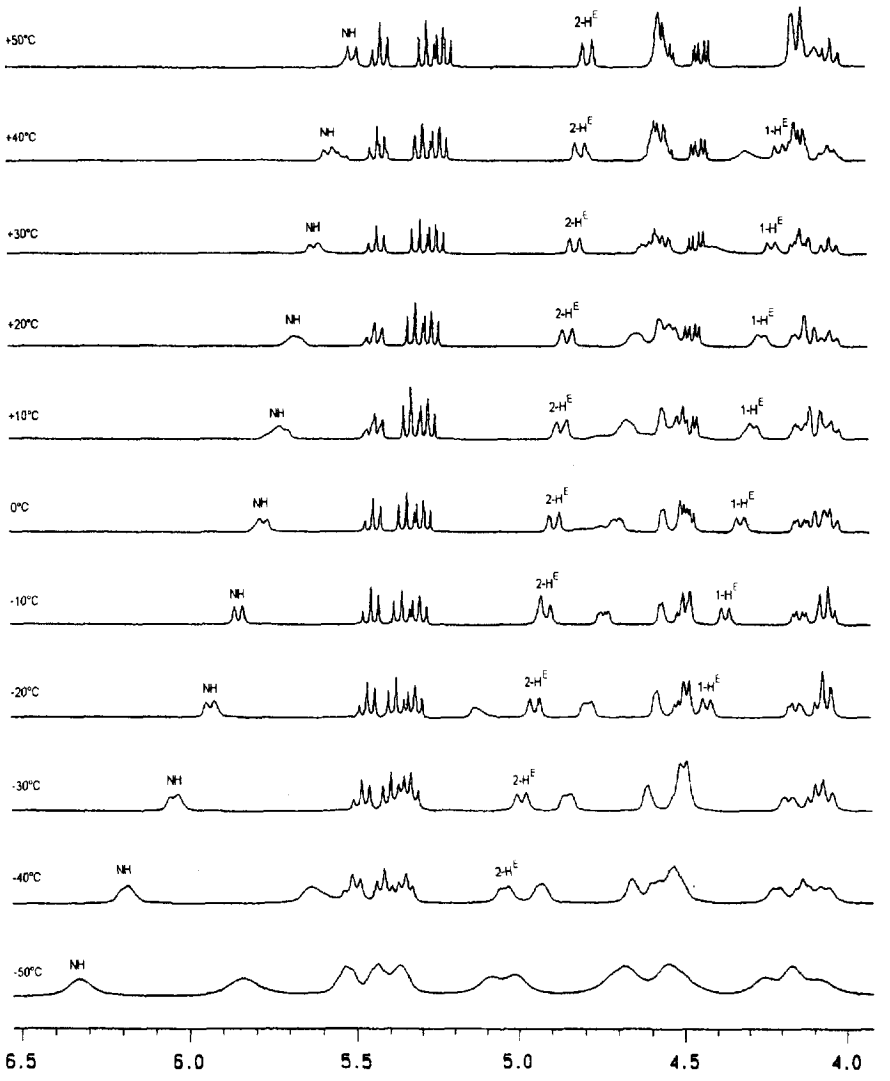


Figure 2. Temperature dependent ^{1}H NMR spectrum of **10a** (δ = 4.0-6.5 region)

Whereas in **10a** ring E adopts the $^4C_1$ conformation ($J_{1E,2E}$ = 1.5 Hz, $J_{2E,3E}$ = 4.2 Hz) in the benzyl analogue **10b** obviously the $^1C_4$ conformation prevails ($J_{1E,2E}$ = 9.9 Hz, $J_{2E,3E}$ = 2.9 Hz). For the sulfonamidoglycosylation the substituents at C-1 and C-2 must be antiperiplanar. We were, therefore, interested to study the dynamic properties of both **10a** and **10b**. The results for **10a** are shown in Figure 2. Conformational equilibria have been

identified by running NMR spectra in the temperature range of -50°C to + 50°C. Coalescence phenomena are evident for NH and 1-H^E. Since 2-H^E does not show such a coalescence the conformational change must be a local phenomenon, and we believe that the sulfonamide group is responsible for it. A similar process has been observed for **10b**. In this case, too, a change in the ring conformation can be excluded in the temperature range investigated (-50°C→50°C).[15] In Figure 2 the expected temperature dependence of the NH proton chemical shift is observed as well as for the water signal ($\delta \approx 5.85$ at -50°C). Interestingly, at low temperatures only a single set of resonances is observed indicating that the second conformer is present only at low concentrations. As will be described below the formation of the N-sulfonylaziridine intermediate in the Danishefsky route is not hampered by fact that **10b** exists mainly in the $^1C_4$ conformation with the substituents at C-1 and C-2 in a diequatorial disposition.

Danishefsky has reported that there are cases where the iodosulfonamides themselves are poor donors in glycosylation reactions. To circumvent these problems the iodosulfonamides were converted into ethyl 2-sulfonamido-2-deoxy-β-thioglycosides which then were used as glycosyl donors after activation with methyl triflate.[16] We explored a different approach and converted iodosulfonamide **10b** via the sulfonylaziridine intermediate into **9** by treatment with aqueous lithium hydroxide in THF (95% yield). **9** was then submitted to the Schmidt glycosylation reaction.[17] Thus, **9** reacted with trichloroacetonitrile in the presence of DBU to furnish **11** (91% yield) which on exposure to the galacturonamide derivative **12** and trimethylsilyltriflate yielded the desired trisaccharide **13** ($\alpha:\beta = 1:4$) in 60 % yield.

Interestingly, the FAB mass spectra of cellobial and its derivatives **7a** and **7b**, and of many of the benzyl protected compounds displayed peaks (formally) at $M^{\cdot}$ and $[M-H]^{\cdot}$, besides $[M+H]^{\cdot}$.[18] At least in the case of cellobial, **7a**, and **7b** according to MIKE analyses these ions are derived from $[M+H]^+$ by loss of a hydrogen atom and of H_2, respectively.

EXPERIMENTAL

General

For flash chromatography (FC), see ref.[19] For all other methods, see ref.[2]. The fragments in the mass spectra are named as introduced in ref.[1]. Benzyl protons and carbons of the individual benzyl group are indicated as a,b,c.....when the connectivity was determined by C,H COSY spectra, for other correlations arbitrarily the peak numbers of the ^{13}C NMR spectra are used. CH_2(a) and CH_2(b) refers to the 2-trimethylsilylethyl protecting group. If not stated otherwise the matrix for the FAB mass spectra was 3-nitrobenzylalcohol.

N-[3,6-Di-O-acetyl-4-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-2-deoxy-2-iodo-α-D-manno-pyranosyl]-2-(trimethylsilyl)-ethanesulfonamide (10a)

To a stirred suspension of **7a** (509 mg, 0.91 mmol), sulfonamide **8** (178 mg, 1.02 mmol), and powdered 4Å molecular sieves in CH_2Cl_2 (5 mL) at 40°C a solution of $I(sym\text{-}coll)_2ClO_4$ (789 mg, 1.68 mmol) in CH_2Cl_2 (7 mL) was added. The mixture was stirred at 40°C for 3 h and then filtered. The residue was washed with CH_2Cl_2 (4x30 mL). The combined organic solutions were washed with sat. aq. $Na_2S_2O_3$ (3x), with sat. aq. $CuSO_4$, and water. Drying ($MgSO_4$), filtration, solvent evaporation and MPLC (petrol - ethyl acetate 1:1) provided pure **10a** (340 mg, 58% based on consumed **7a**). 130 mg (0.23 mmol) of **7a** were recovered.- ^1H NMR (400 MHz, $CDCl_3$): δ = 5.31 (d, $J_{1E,\,NH}$ = 10.5 Hz, NH), 5.15 (t, $J_{2C,\,3C} = J_{3C,\,4C}$ = 9. 5 Hz, 3-H^C), 5.03 (t, $J_{4C,\,5C}$ = 9.5 Hz, 4-H^C), 4.90 (dd, 2-H^C), 4. 69 (dd, $J_{1E,\,2E}$ = 1.5 Hz, $J_{2E,\,3E}$ = 4.2 Hz, 2-H^E), 4.6 (dd, $J_{5C\text{ or }E,\,6C\text{ or }E}$ = 4.6 Hz, $J_{6C\text{ or }E,\,6'C\text{ or }E}$ = 12.2 Hz, $6^{C\text{ or }E}$-H), 4.56 (d, $J_{1C,\,2C}$ = 8.1 Hz, 1-H^C), 4.42 (dd, $J_{3E,\,4E}$ = 9.1 Hz, 3-H^E), 4.30 (dd, $J_{5E\text{ or }C,\,6E\text{ or }C}$ = 5.1 Hz, $J_{6E\text{ or }C,\,6'E\text{ or }C}$ = 12.5 Hz, $6^{E\text{ or }C}$-H), 4.08 (dd, 1-H^E), 4.03 (dd, $6^{E\text{ or }C}$ -H'), 3.96 (dd, $6^{C\text{ or }E}$ -H'), 3.92 (t, $J_{4E,\,5E}$ = 9.5 Hz, 4-H^E), 3.68 (ddd, $J_{5E\text{ or }C,\,6'E\text{ or }C}$ = 2.2 Hz, 5-$H^{E\text{ or }C}$), 3.62 (ddd , $J_{5C\text{ or }E,\,6'C\text{ or }E}$ = 2.0 Hz, 5-$H^{C\text{ or }E}$), 3.00 - 3.09 (m, CH_2(a)), 2.12 - 1.96 (6 * s, OAc signals), 0.90 - 1.10 (m, CH_2(b)), 0.00 (s, $Si(CH_3)_3$).- ^{13}C NMR (100.6 MHz, C,H COSY, $CDCl_3$): δ = 170.4 - 169.0 (OAc signals), 100.5 (C-1^C), 79.5 (C-1^E), 75.2 (C-$5^{C\text{ or }E}$), 74.6 (C-4^E), 72.6 (C-3^C), 71.7 (C-$5^{E\text{ or }C}$), 71.4 (C-2^C), 71.0 (C-3^E), 67.9 (C-4^C), 61.9 (C-$6^{E\text{ or }C}$), 61.3 (C-$6^{C\text{ or }E}$), 51.8 (CH_2(a)), 38.9 (C-2^E), 20.4 - 20.7 (OAc), 10.1 (CH_2(b)), -2.2 ($Si(CH_3)_3$).- $C_{29}H_{46}INO_{17}SSi$ (867.72, 867.13), FAB MS: m/z = 868.1 ($[M+H]^+$), 740.2 ($[M\text{-}HI]^+$), 331 ($[c]^+$).

3,6-Di-O-benzyl-4-O-(2,3,4,6-tetra-O-benzyl-β-D-glucopyranosyl)-1,5-anhydro-2-deoxy-D-gluco-hex-1-enitol (7b)

To a solution of cellobial (20.00 g, 0.07 mol) in DMSO (250 mL) sodium methylsulfinylmethide (2 mol/L in DMSO, 200 mL, 0.400 mol) was added within 1 h. Then benzyl chloride (100 mL) was added at such a rate that a reaction temperature of 40°C was maintained (3 h, colour change greenish→red-violet). After 15 h to the yellow reaction mixture first methanol (50 mL) and then ice-water (20 mL) were added. Volatiles were removed at 100°C / 10^{-2} mbar. The residue was taken up in $CHCl_3$ (500 mL) and the solution was washed with sat. aq. NH_4Cl. After solvent evaporation to the oily residue water was added and the mixture was first sonified and then lyophilized. This process was repeated 5 times. The solified product was purified by LC (petrol - ethyl acetate 9:1) to provide **7b** (24.83 g, 45%).- ^1H NMR (400 MHz, $CDCl_3$): δ = 6.39 (d, $J_{1E,\,2E}$ = 6.4 Hz, 1-H^E), 4.82 (dd, partially hidden, 2-H^E), 4.52 (d, $J_{1C,\,2C}$ = 7.8 Hz, 1-H^C), 4.25 - 4.20 (m, 1H), 4.16 - 4.11 (m, 1H, correlates with *7*), 4.09 - 4.06 (m, 1H, correlates with *4*), 3.79 (dd, $6^{C\text{ or }E}$-H), 3.62 - 3.58 (m, 3H, $6^{C\text{ or }E}$-H', CH_2-$6^{E\text{ or }C}$), 3.55 - 3.50 (m, 2H, correlate with *15*, *13*), 3.40 - 3.35 (m, 2H, correlate with *14*, *8*), benzyl group signals at: 7.15 - 7.35 (m, Ar-H); 4.85, 4.71 ($CH_2^{benzyl\ (f)}$, AB); 4.80, 4.60 ($CH_2^{benzyl\ (d)}$, AB); 4.74, 4.47 ($CH_2^{benzyl\ (e)}$, AB); 4.54 ($CH_2^{benzyl\ (a)}$, AB); 4.43 ($CH_2^{benzyl\ (b)}$, AB); 4.45, 4.38 ($CH_2^{benzyl\ (c)}$, AB).- ^{13}C-NMR (100.6 MHz, C,H COSY, DEPT, $CDCl_3$): δ = 144.1 (C-1^E), 102.2 (C-1^C), 99.1 (C-2^E), 84.1 (CH, *15*), 81.5 (CH, *14*), 77.2 (CH, *13*), 75.4 (CH, *12*), 74.3 (CH, *8*), 72.90 (CH, *7*), 71.2 (CH, *4*), 68.4 (C-$6^{E\text{ or }C}$, *2*), 67.2 (C-$6^{C\text{ or }E}$, *1*), benzyl group signals at: 138.2 - 137.4 (Ar-C^{i}'s), 127.9 - 126.9 (Ar-C's), 75.1 ($CH_2^{benzyl\ (f)}$), 74.4 ($CH_2^{benzyl\ (e)}$), 74.3 ($CH_2^{benzyl\ (d)}$), 72.85 ($CH_2^{benzyl\ (c)}$), 72.7

($CH_2^{benzyl\ (b)}$), 69.5 ($CH_2^{benzyl\ (a)}$).- $C_{54}H_{56}O_9$ (849.03, 848.39), FAB MS (MIKE-spectra): m/z = 871.2 ($[M+Na]^+$), 849.0 ($[M+H]^+$), 848.0 ($[M+H-H^\bullet]^+$), 847.2 ($[M+H-H_2]^+$), 741.2 ($[M+H-BnOH]^+$).

N-[3,6-Di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl)-2-deoxy-2-iodo-α-D-manno-pyranosyl]-(2-trimethylsilyl)ethanesulfonamide (10b)

To a suspension of **7b** (20.68 g, 0.024 mol), sulfonamide **8**, and 4Å molecular sieves (14.00 g) in CH_2Cl_2 (120 mL) solid $I(sym\text{-}coll)_2ClO_4$ (49.00 g, 0.104 mol) was added. The mixture was stirred at 0°C for 5 h. Work-up was perfomed as described for **7a**→**10a**. FC (petrol - ethyl acetate 10:1 ⇒ 3:1) furnished **10b** (18.64 g, 66%).- IR ($CHCl_3$): 3375 cm^{-1} (NH).- ^1H NMR (400 MHz, H,H COSY, $CDCl_3$): δ = 5.18 (t, broad, $J_{1E,\ NH} = J_{1E,\ 2E} = 9.9$ Hz, after NH→ND exchange: d, $J_{1E,\ 2E} = 9.9$ Hz, 1-H^E) 4.85 (d, broad, NH), 4.38 (dd, partially hidden, $J_{2E,\ 3E} = 2.9$ Hz, 2-H^E), 4.25 (d, $J_{1C,\ 2C} = 7.7$ Hz, 1-H^C), 4.23 - 4.18 (m, 5-H^C) , 4.15 - 4.12 (m, 3-H^E), 3.90 - 3.84 (m, 6^C-H), 3.63 - 3.61 (m, partially hidden, 4-H^E, CH_2-6^E), 3.59 - 3.52 (m, partially hidden, 4H, including 3-H^C, 4-H^C, 6^C-H'), 3.44 - 3.39 (m, $J_{2C,\ 3C} \approx 7.7$ Hz, 2-H^C), 3.38 - 3.33 (m, 5-H^E), 3.12 - 2.92 (m, CH_2(a)), 1.02 - 0.95 (m, CH_2(b)), - 0.12 (s, TMS), benzyl group signals at: 7.30 - 7.20 (m, Ar-H); 4.88, 4.77 ($CH_2^{benzyl\ (a)}$, AB); 4.85, 4.69 ($CH_2^{benzyl\ (b)}$, AB); 4.83, 4.54 ($CH_2^{benzyl\ (c)}$, AB); 4.64, 4.51 ($CH_2^{benzyl\ (d)}$, AB); 4.54 ($CH_2^{benzyl\ (e)}$, AB); 4.42, 4.47 ($CH_2^{benzyl\ (f)}$, AB).- ^{13}C NMR (100.6 MHz, C,H COSY, DEPT, $CDCl_3$): δ = 103.3 (C-1^C), 84.2 (C-3^C or C-4^C), 81.6 (C-2^C), 79.3 (C-3^E), 78.2 (C-1^E), 77.3 (C-4^C or C-3^C), 76.7 (C-5^C), 74.5 (C-5^E), 74.3 (C-4^E), 68.6 (C-6^E), 67.1 (C-6^C), 50.6 (CH_2(a)), 29.6 (C-2^E), 10.1 (CH_2(b)), -2.3 ($Si(CH_3)_3$), benzyl group signals: 138.2 - 137.6 (5 Ar-C''s), 128.1 - 127.4 (Ar-C's), 75.4 ($CH_2^{benzyl\ (a)}$), 74.8 ($CH_2^{benzyl\ (b)}$), 74.6 ($CH_2^{benzyl\ (c)}$), 73.6 ($CH_2^{benzyl\ (d)}$), 73.3 ($CH_2^{benzyl\ (e)}$), 73.1 ($CH_2^{benzyl\ (f)}$).- $C_{59}H_{70}INO_{11}SSi$ (1156.26, 1155.33), FAB MS: m/z = 1178.3 ($[M+Na]^+$), 1154.2 ($[M+H-H_2]^+$, 523.2 ($[c]^+$).- HR MS: $[M+Na]^+$: calc 1178.3381, found 1178.3380.

3,6-Di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl)-2-deoxy-2-(2-trimethylsilylethane-sulfonylamino)-α-D-glucose (9)

To a solution of **10b** (50 mg, 0.04 mmol) in 2.5:1 THF - H_2O (1.5 mL) at 0°C slowly lithium hydroxide (1 mol/L in water, 65 µl) was added and the mixture was stirred at 0°C for 2 h. Then a further portion of the lithium hydroxide solution (90 µl) was added and the mixture was now stirred at 22°C for 4 h. NH_4Cl (100 mg) was added. After solvent evaporation the residue was extracted with CH_2Cl_2 and the extract filtered through Florisil®. After solvent evaporation pure (TLC petrol - ethyl acetate 2:1) **9** (43 mg, 95 %) was obtained.- IR (KBr): 3607 and 3560 - 3200 cm^{-1} (OH, NH).- ^1H NMR (400 MHz, $CDCl_3$), characteristic signals: δ = 5.37 - 5.31 (m, after OH→OD exchange: d, $J_{1E,\ 2E} = 3.7$ Hz, 1-H^E), 4.49 (d, $J_{2E,\ NH} = 10.3$ Hz, NH), 4.46 (d, $J_{1C,\ 2C} \approx 11.0$ Hz, 1-H^C), 3.43 - 3.35 (m, after OH→OD exchange: dd, $J_{2E,\ 3E} = 10.3$, 2-H^E), 3.05 (broad s, exchangable with D_2O), 2.90 - 2.65 (m, CH_2(a)), 0.90 - 0.78 (m, CH_2(b)), -0.21 (s, $Si(CH_3)_3$).- ^{13}C NMR (100.6 MHz, APT, C,H COSY, $CDCl_3$): δ = 103.1 (C-1^C), 93.0 (C-1^E), 85.3 (CH), 83.2 (CH), 78.5 (CH), 78.0 (CH), 77.2 (CH), 76.1 (CH_2), 75.6 (CH_2), 75.5 (CH_2), 75.3 (CH_2), 73.9 (CH_2), 73.8 (CH_2), 71.2 (CH), 69.4 (CH_2), 68.3 (CH_2), 57.7 (C-2^E), 50.3 (CH_2(a)), 10.4 (CH_2(b)), - 1.7 ($Si(CH_3)_3$), 139.3 - 138.3 (Ar-C''s), 129.0-128.0 (Ar-C's).- $C_{59}H_{71}NO_{12}SSi$ (1046.37, 1045.45), FAB MS: m/z = 1068.1 ($[M+Na]^+$).

O-[3,6-Di-O-benzyl-4-O-(2,3,4,6-tetra-O-benzyl-β-D-glucopyranosyl)-2-deoxy-2-(2-trimethylsilylethanesulfonylamino)-α-D-glucopyranosyl]-trichloroacetimidate (11)

A solution of **9** (107 mg, 0.1023 mmol), trichloroacetonitrile (102 µl, 1.02 mmol) and DBU (4 µl, 0.03 mmol) in CH_2Cl_2 (2 mL) was stirred at 0°C for 3.5 h. Solvent evaporation and FC (petrol - ethyl acetate 8:1 + 1% NEt_3) provided **11** (110 mg, 91 %, TLC: petrol - $CHCl_3$ - CH_3OH 8:8:0.3), a very sensitive compound for which only a limited set of analytical data could be obtained.- ^1H NMR (200 MHz, $CDCl_3$), characteristic signals: δ = 8.75 (s, C=NH), 6.45 (broad s, 1-H^E), 3.00 - 2.70 (m, CH_2(a)), 1.10 - 0.80 (m, CH_2(b)), 0.08 (s, $Si(CH_3)_3$).- ^{13}C NMR (100.6 MHz, $CDCl_3$), characteristic signals: δ = 160.8 (C=NH), 103.0 (C-1^C), 96.8 (C-1^E), 85.3, 83.0, 78.4, 78.4, 76.8, 76.3, 75.4, 75.3, 74.1, 74.0, 69.4, 67.7, 57.0 (C-2^E), 50.6 (CH_2(a)), 10.6 (CH_2(b)), -1.6 ($Si(CH_3)_3$), 138.8 - 138.2 (Ar-C''s), 129.2 - 128.1 (Ar-C's).- $C_{61}H_{71}Cl_3N_2OSSi$ (1190.76, 1188.35).

Allyl 2-O-[3,6-di-O-benzyl-4-O-(2,3,4,6-tetra-O-benzyl-β-D-glucopyranosyl)-2-deoxy-2-(2-trimethylsilylethanesulfonylamino)-D-glucopyranosyl]-3,4-O-isopropylidene-α-D-galacto-pyranosiduronamide (13), 1:4 mixture of 1^E-α-and -β-anomers

A mixture of **11** (50 mg, 0.04 mmol), glycosyl acceptor **12** (16 mg, 0.06 mmol), 4 Å molecular sieves (50 mg), hexane (150 µL), and CH_2Cl_2 (200 µL) was stirred at 25°C for 1 h. At -20°C within 2 h TMSOTf (1 mol/L in toluene, 2*9 µL) was added and the mixture was stirred at 0°C for 2 h. Then triethylamin (25 µL) was added and the solvents were evaporated. FC (petroleum ether - ethyl acetate 5:1) furnished **13** (33 mg, 60 %) in an α : β ratio of 1:4. IR (KBr): 3600 - 3200 (NH), 1684, 1653, 1636, 1630 cm^{-1}.- ^1H NMR (400 MHz, $CDCl_3$), only the signals of the ß anomer are reported: δ = 7.30 - 7.20 (m, Ar-H) 6.42 (broad s, $CONH_2$), 5.43 (broad s, $CONH_2$), 5.01 (d, $J_{1F,\,2F}$ = 3.4 Hz, 1-H^F), 4.84 (d, J = 11.0 Hz, 1H), 4.80 - 4.68 (m, 6H), 4.52 - 4.36 (m, 4H), 4.42 - 4.37 (m, 3H), 4.23 (dd, $J_{3F,\,4F}$ = 5.4 Hz, $J_{4F,\,5F}$ = 8.3 Hz, 3-H^F), 4.00 - 3.95 (m, 1H), 3.85 (dd, J = 8.3 Hz, J = 3.5 Hz, 1H), 3.73 (dd, J = 8.7 Hz, J = 4.6 Hz, 1H), 3.65 (dd, J = 10.0 Hz, J = 1.5 Hz, 1H), 3.62 - 3.38 (m, 9H), 3.30 - 3.08 (m, CH_2(a)), 1.40 and 1.30 (2*s, O-C($C\underline{H}_3$)$_2$-O), 1.05 - 0.80 (m, CH_2(b)), - 0.20 ($Si(CH_3)_3$), allyl group signals at 5.82 (m, $OCH_2C\underline{H}=CH_2$), 5.26 (m, 1H of $OCH_2CH=C\underline{H}_2$), 5.12 (m, 1H of $OCH_2CH=C\underline{H}_2$), 4.05 (ddt, $OC\underline{H}_2CH=CH_2$)).- ^{13}C NMR (100.6 MHz, APT, C,H COSY, $CDCl_3$): δ = 170.4 ($CONH_2$), 109.7 (O-$\underline{C}(CH_3)_2$-O), 103.0 (C-1^C), 102.0 (C-1^E), 98.1 (C-1^F), 84.8 (CH), 82.6 (CH), 79.1 (CH), 78.0 (CH), 76.2 (CH), 75.6 (CH), 75.4 (CH), 73.7 (CH), 68.8 (C-6), 68.7 (C-6), 68.3, 57.7 (C-2^E), 50.9 (CH_2(a)), 28.3 and 26.6 (O-C($\underline{C}H_3$)$_2$-O), 10.2 (CH_2(b)), -1.8 ($Si(CH_3)_3$), allyl group signals at 133.3 ($OCH_2\underline{C}H=CH_2$), 118.2 ($OCH_2CH=\underline{C}H_2$), 69.6 ($O\underline{C}H_2CH=CH_2$), benzyl group signals at 138.6 - 138.0 (Ar-C''s),128.8 - 127.5 (Ar-C's), 75.6, 75.1, 75.0, 73.3, 72.3 (CH_2).- FAB MS: m/z 1339.5 ($[M+K]^+$), 1323.6 ($[M+Na]^+$), 1301.6 ($[M+H]^+$), 779.1 ($[M+H-c]^+$), 523 ($[c]^+$).- $C_{71}H_{88}N_2O_{17}SSi$ (1301.63, 1300.56), calc C 65.52, H 6.81, N 2.15, found C 65.40, H. 6.82, N 2.19.- HR-MS $[M+Na]^+$: calc 1323.5470, found 1323.5490.

Acknowledgements - We wish to thank K.Floeder and S.Hamm for skillful assistance and Dr.M.Lampilas (Roussel Uclaf) for helpful discussions. Financial support by the Deutsche Forschungsgemeinschaft (We 595/22-1 and Innovationskolleg „Chemisches Signal und biologische Antwort"), the Fonds der Chemischen Industrie, Roussel Uclaf, and the Hoechst AG is gratefully acknowledged.

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Dedicated with great admiration to Professor Hans Paulsen on the occasion of his 75th birthday

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(*Received in Germany* 28 *October* 1996; *accepted* 29 *November* 1996)