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ASYMMETRIC INDUCTION IN [2+2]CYCLOADDITION OF CHLOROSULFONYL ISOCYANATE TO 1,2-*O*-ISOPROPYLIDENE-3-*O*-VINYL-GLYCOFURANOSES

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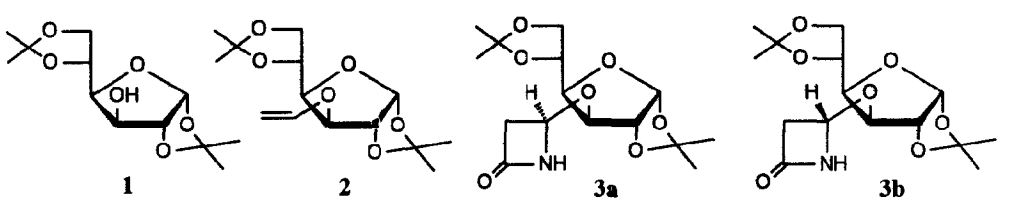
Abstract: The asymmetric [2+2]cycloaddition of chlorosulfonyl isocyanate to 1,2-*O*-isopropylidene-3-*O*-vinyl-glycofuranoses is presented. Bulky substituent at the C-4 carbon atom promotes excellent stereoselectivity affording (R) configuration at the C-4' carbon atom of the azetidinone ring. Intramolecular cyclization in compounds **9** or **12** provides diastereomeric cephem **20** and **21**.

In recent years carbohydrates have gained much attention as chiral auxiliaries in stereoselective synthesis,[1] Among variety of sugar derivatives diacetone glucose (**1**), owing to its accessibility played a special role.[2]

Five years ago we reported the formation of a β-lactam ring *via* asymmetric [2+2]cycloaddition of tosyl isocyanate to vinyl ether of diacetone glucose (**2**).[3] The (4R) diastereomer of azetidinone **3a** has been obtained predominantly with diastereoselectivity 86:14. However, removal of *N*-tosyl substituent with sodium in liquid ammonia, in order to form a stable product, proceeded, in low yield. Trichloroacetyl isocyanate which at that time has successfully been used by us to obtain β-lactams from glycals, when reacted with **2** gave exclusively [4+2]cycloadduct and showed no diastereoselectivity.[3]

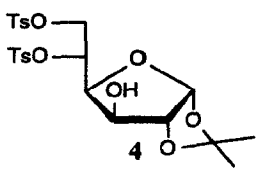


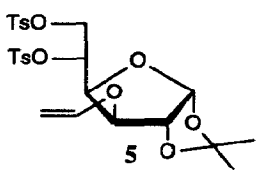
1 **2** **3a** **3b**

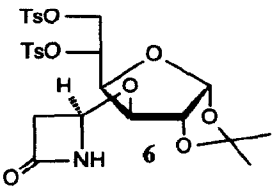
Recently we have found that storage of chlorosulfonyl isocyanate over potassium, sodium or calcium carbonate and the addition of these bases to the reaction mixture have enabled to perform its [2+2]cycloadditions with reactive olefins,[4] which, owing to the acidity of the commercially available reagent

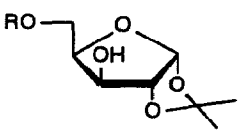
so far gave negative results. This important observation prompted us to return to the problem of [2+2]cycloaddition of chlorosulfonyl isocyanate to simple sugar vinyl ethers. Our reinvestigation of this cycloaddition had two goals: the first to find conditions that would enhance diastereoselectivity of [2+2]cycloaddition, and allow improvement of the *N*-deprotection of the cycloadduct and the second to find an entry to 1-oxabicyclic β-lactams *via* reconstruction of the adduct thus obtained. The latter goal should offer an alternative route to the commonly used for clavam synthesis, consisting in condensation of readily available 4-acetoxyazetidinone with sugar alcohols.[5] Such condensation has been known to give usually a moderate asymmetric induction.[5]

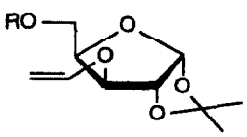
For present studies as model compounds we selected 3-*O*-vinyl derivatives of 1,2-*O*-isopropylidene-α-D-glucofuranose (**2,5**) and α-D-xylofuranose (**8, 11, 14**).

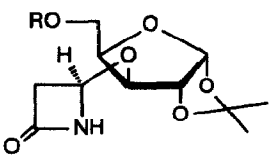


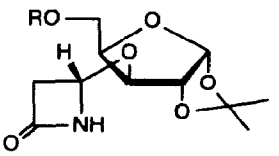






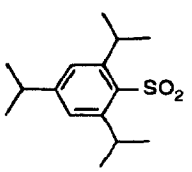


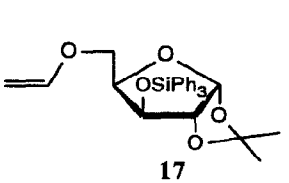




R= Ts	**7**	**8**	**9a**	**9b**
R= TIBS	**10**	**11**	**12a**	**12b**
R= $SiPh_3$	**13**	**14**	**15**	
R= H		**16**		

TIBS =





17

Compounds **5**, **8**, and **11** were obtained from proper 3-hydroxy precursors **4**, **7**, and **10** using a known mercury acetate catalyzed trans etherification method.[6] Vinyl eter **5** contaminated with about 50% of 3-*O*-(1'-butoxyethyl)-1,2-*O*-isopropylidene-4,5-di-*O*-tosyl-α-D-glucofuranose and was used for cycloaddition as a mixture. In the case of the vinylation of compound **13** the product **14** was contaminated with its regioisomer **17** (30%) which showed similar chromatographical mobility as the main product and was difficult to separate. Pure **14** can be obtained from **8** by a two step transformation, which consisted of the removal of the tosyl protection by a sodium in liquid ammonia reduction to afford **16** followed by a desired protection of the

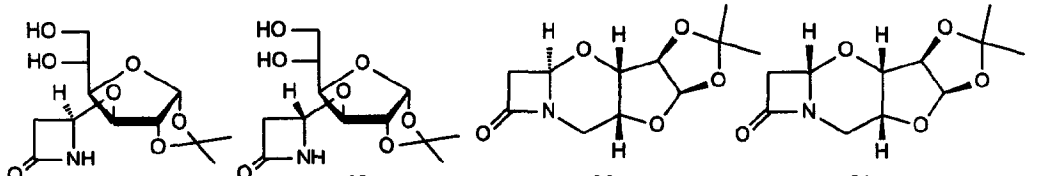
terminal hydroxymethyl group. This procedure can be used for synthesis of vinyl ethers having an acid labile substituent present in their substrates.

High reactivity of chlorosulfonyl isocyanate towards simple vinyl ethers particularly in polar aprotic solvents restricted reaction conditions to low temperature and to non polar solvents. Reaction of compound **2** with chlorosulfonyl isocyanate in anhydrous toluene at -40°C afforded lower asymmetric induction than with tosyl isocyanate, but *N*-deprotection could be came out under milder conditions - Red-Al reduction.[7] The main drawback of chlorosulfonyl isocyanate is linked with its high reactivity towards many functional groups. In our case, 5,6-*O*-isopropylidene or triisopropylbenzenesulfonyl TIBS groups were shown to be labile in the presence of chlorosulfonyl isocyanate.

The results of [2+2]cycloaddition of chlorosulfonyl isocyanate to 3-*O*-vinyl furanoses **2**, **5**, **8**, **11**, and **14** are shown in Table 1.

The configurations of diastereomers **3** and **6** were correlated to the configuration of compound **18** whose structure was proved by X-ray measurement.[8]

Compound **18** and its 4'-epimer **19** were obtained by 5,6-deprotection of β-lactams **3**. Configurations of compounds **9** and **12** were proved by transformation of these compounds into cephams **20** and **21**. This intramolecular alkylation was carried out in a very good yield using a two - phase system (anhydrous potassium carbonate/tetraammonium bromide) in acetonitrile. Structure and configuration of **20** and **21** were determined by the X-ray analysis,[8] and NOE measurements.[8]



Desilylation - tosylation procedure allowed to proved configuration of the single product **15a**.

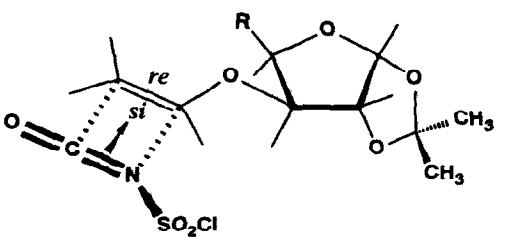
The results presented in Table 1 show that stereoselectivity of cycloaddition is sterically controlled. The large substituent at the C-4 carbon atom of the furanose ring blocks the isocyanate entry from the *re* side (Scheme 1) and affords full stereoselectivity in the case of **5** and **14**. The comparison of the face-discrimination found for addition of chlorosulfonyl isocyanate to **8** and to **11** is particularly interesting. Lower face - discrimination found for **8**, excludes complexation of the nucleophilic olefin by the electrophilic aromatic ring as an element that helps to decide on direction of asymmetric induction and its value. It is obvious that if such complexation occurs, it should be stronger for the more accessible and more electrophilic tosyl substituent. High stereoselectivity found for **15** could also be assigned to the steric effect rather than to the complexation of the double bond, although stronger complexation of the vinyl group by 6-*O*-tosyl than by 5-*O*-tosyl substituent should be taken into consideration.

Table 1. Diastereoselective [2+2]cycloaddition of chlorosulfonyl isocyanate to 3-*O*-vinyl ethers of 1,2-*O*-isopropylidene-glycofuranoses **2**, **5**, **8**, **11**, and **14**

Compound	T (°C)	Time (h)	Products	Diastereoselectivity	Yield (%)
2	-40	1	**3a:3b**	3:1	20
2	-70	3	**3a:3b**	4:1	20
5	-40	1.5	**6**	-	60*
8	-40	1.5	**9a:9b**	2:1	50
11	-40	2	**12a:12b**	3.3:1	25
14	-70	2	**15**	-	50

* calculated for pure substrate

Scheme 1



Readily available substrates, high asymmetric induction, and possible further transformations make [2+2]cycloaddition of chlorosulfonyl isocyanate to 3-*O*-vinyl ethers derived from 1,2:5,6-di-*O*-isopropylidene-D-glucofuranose (**1**) a very attractive tool for the synthesis of 1-oxacephams having potential biological activity.

Experimental

Melting points are uncorrected, optical rotations were measured with a JASCO Dip-360 digital polarimeter. IR spectra were taken with a Perkin-Elmer FT-IR-1600 spectrophotometer. ^{1}H NMR spectra were recorded with Varian Gemini 200 and Bruker AM 500 spectrometers. Column chromatography was performed on Merck Kieselgel (230-400 mesh).

Compounds **5**, **8**, **11**, and **14** were obtained according to the known procedure.[6]

1,2-*O*-isopropylidene-5,6-di-*O*-tosyl-3-O-vinyl-α-D-glucopyranose (**5**). IR ($CHCl_3$): 1621 cm^{-1}; ^{1}H NMR ($CDCl_3$) selected absorptions taken from the contaminated substrate: 4.17 (dd, 1H, *J* 2.6, 6.8 Hz, vinyl),

4.54 (d, 1H, $J_{1,2}$ 3.7 Hz, H-2), 5.77 (d, 1H, H-1), 6.22 (dd, 1H, *J* 6.8, 14.4 Hz, vinyl); MS (EI, HR) m/z: (M^+-CH_3) calcd for $C_{24}H_{27}O_{10}S_2$: 539.10456. Found: 539.10407.

1,2-*O*-isopropylidene-5-*O*-tosyl-3-*O*-vinyl-α-D-xylofuranose (8). mp. 128-129°C; $[\alpha]_D$ -19.9° (*c* 1.2, CH_2Cl_2); IR ($CHCl_3$): 1622 cm^{-1}; ^1H NMR ($CDCl_3$): 1.29, 1.47 (2s, 6H, isoprop.), 4.14 (dd, 1H, *J* 2.6, 6.7 Hz, vinyl), 4.19 (dd, 1H, *J* 6.3, 10.3 Hz, H-5), 4.25 (dd, 1H, *J* 5.9, 10.3 Hz, H-5'), 4.31 (d, 1H, $J_{3,4}$ 3.8 Hz, H-3), 4.33 (dd, 1H, *J* 2.6, 14.4 Hz, vinyl), 4.45 (sext, 1H, H-4), 4.54 (d, 1H, $J_{1,2}$ 3.8 Hz, H-2), 5.84 (d, 1H, H-1), 6.24 (dd, 1H, *J* 6.7, 14.4 Hz, vinyl): MS (EI, HR) m/z: (M^+-CH_3) calcd for $C_{16}H_{19}O_7S$: 355.08514. Found: 355.08500.

1,2-*O*-isopropylidene-5-*O*-triisopropylbenzenesulfonyl-3-*O*-vinyl-α-D-xylofuranose (11). $[\alpha]_D$ -11.6° (*c* 2.2, CH_2Cl_2); IR ($CHCl_3$): 1622 cm^{-1}; ^1H NMR ($CDCl_3$): 1.30, 1.47 (2s, 6H, isopr.), 2.9 (septet, 1H, *p*-*i*-Pr), 4.13 (septet, 2H, *o*-*i*-Pr), 4.16 (dd, 1H, vinyl), 4.20 (dd, 1H, H-5), 4.33-4.38 (m, 3H, H-3,5', vinyl), 4.58 (d, 1H, $J_{1,2}$ 3.8 Hz, H-2), 4.88 (m, 1H, H-4), 5.87 (d, 1H, H-1), 6.31 (dd, 1H, *J* 6.8, 14.3 Hz, vinyl); MS (EI, HR) m/z: (M^+-CH_3) calcd for $C_{24}H_{35}O_7S$: 467.21034. Found: 467.21050.

1,2-isopropylidene-5-*O*-triphenylsilyl-3-*O*-vinyl-α-D-xylofuranose (14): $[\alpha]_D$ -42.5° (*c* 0.1, CH_2Cl_2); IR ($CHCl_3$): 1621 cm^{-1}; ^1H NMR ($CDCl_3$): 1.30, 1.48 (2s, 6H, izopr.), 4.02 (m, 2H, H-5,5'), 4.09 (dd, 1H, *J* 2.3, 6.8 Hz, vinyl), 4.35 (dd, 1H, *J* 2.3, 14.4 Hz, vinyl), 4.38-4.47 (m, 2H, H-3,4), 4.57 (d, 1H, $J_{1,2}$ 3.9 Hz, H-2), 5.87 (d, 1H, H-1), 6.28 (dd, 1H, *J* 6.8, 14.4 Hz, vinyl); MS (EI, HR) m/z: (M^+-CH_3) calcd for $C_{27}H_{27}O_5Si$: 459.16277. Found: 459.16270.

17: ^1H NMR ($CDCl_3$) selected signals taken from the spectrum of the mixture of **14** (70%) and **17** (30%): 1,20, 1.43 (2 s, 6H, isopr.), 3.83 (dd, 1H *J* 5.6, 10.0 Hz, H-5), 3.91 (dd, 1H, *J* 6.5, 10.0 Hz, H-5'), 3.95 (d, 1H, *J* 2.3, 6.8 Hz, vinyl), 4.47 (d, 1H, $J_{3,4}$ 2.7 Hz, H-3), 5.96 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 6.39 (dd, 1H, *J* 6.7, 14.4 Hz, vinyl).

1,2-*O*-isopropylidene-5-*O*-triphenylsilyl-3-*O*-vinyl-α-D-xylofuranose (14) from **8**. To a solution of sodium (0.74 g, 32 mmol) in liquid ammonia (200 ml) compound **8** (3.0 g, 8.1 mmol) in dry THF (10 ml) was added dropwise. Reduction was continued at -33°C for 1.5 h. Subsequently ammonium chloride (5 g) was added and ammonia was allowed to evaporate. The reaction mixture was treated with water (20 ml) and extracted with AcOEt. The product was purified by chromatography to afford **16** (1.25 g, 76%); $[\alpha]_D$ -47.0° (*c* 0.3, CH_2Cl_2); ^1H NMR ($CDCl_3$): 1.33, 1.52 (2s, 6H, isopr.), 3.84 (dd, 1H, $J_{4,5}$ 4.9, $J_{5,5'}$ 11.9 Hz, H-5), 3.94 (dd, 1H, $J_{4,5'}$ 5.7, H-5'), 4.19 (dd, 1H, *J* 2.5, 6.8 Hz, vinyl), 4.40 (dd, 1H, *J* 2.5, 14.4 Hz, vinyl), –4.4 (m, 2H, H-3,4), 4.61 (d, 1H, $J_{1,2}$ 3.9 Hz, H-2), 5.95 (d, 1H, H-1), 6.37 (dd, 1H, *J* 6.8, 14.4 Hz, vinyl); MS (ET, HR) m/z: (M^+-15) calcd for $C_9H_{13}O_5$: 201.0763. Found: 201.0762. Compound **16** (0.16 g, 0.8 mmol) was dissolved in CH_2Cl_2 (3 ml) and pyridine (5 ml) and treated dropwise with triphenylsilylchloride (0.3 g, 1.0 mmol) in CH_2Cl_2 (2 ml). The mixture was stirred at room temperature for 20 min and then poured into water and extracted with toluene. The extract was dried and evaporated. The crude product was purified by chromatography to give **8** (0.24, 65%).

[2+2]Cycloaddition of chlorosulfonyl isocyanate to vinyl ethers 2, 5, 8, 11, and 14. To a suspension of anhydrous sodium carbonate (0.15 g) in anhydrous toluene (2 ml) chlorosulfonyl isocyanate (114 μl, 1.3 mmol) was added. The mixture was stirred and upon cooling to -78°C a solution of a vinyl ether **2, 5, 8, 11,** or **14** (1.0 mmol) in toluene (2 ml) was added dropwise. Depending on the vinyl ether the temperature of the mixture was allowed to rise to -40° - 60°C and it was maintained for 20 min -5 h. The suspension was cooled to -78°C, diluted with toluene (6 ml), treated with Red-Al (1.4 ml of a 1M solution in toluene), and left for 15 min whereas the temperature of reaction was maintained. Subsequently the temperature was allowed to rise to -10°C, water (0.5 ml) was added, and the solution was stirred for 45 min. The organic layer was separated, washed, dried, and purified on silica gel to give the respective products.

(4'R) 3-*O*-(azetidin-2'-onyl-4')-1,2-*O*-(isopropylidene-5,6-di-*O*-tosyl-α-D-glucofuranose, (6); 60%; $[\alpha]_D$ -22.9° (*c* 0.6, CH_2Cl_2); IR ($CHCl_3$): 1776 cm^{-1}; ^1H NMR ($CDCl_3$): 1.30, 1.44 (2s, 6H, isopr.), 2.44, 2.47 (2s, 6H, CH_3), 3.02 (dd, 1H, *J* 1.7, 15.5 Hz, H-3'a), 3.22 (ddd, 1H, *J* 3.5, 4.0, 15.5 Hz, H-3'b), 4.00 (dd, 1H, $J_{5,6a}$ 5.6, $J_{6,6a}$ 11.4 Hz, H-6a), 4.20-4.36 (m, 3H, H-3, 4, 6b), 4.54 (d, 1H, $J_{1,2}$ 3.7 Hz, H-2), 5.10 (ddd, 1H, H-5), 5.38 (dd, 1H, *J* 1.7, 4.0 Hz, H-4'), 5.82 (d, 1H, H-1); MS (EI, HR) m/z: $M^{+\cdot}$ calcd for $C_{26}H_{31}NO_{11}S_2$: 597.1338. Found: 597.1336.

(4'R) and **(4'S) 3-*O*-(azetidin-2'-onyl-4')-1,2-*O*-isopropylidene-5-*O*-tosyl-α-D-xylofuranose (9a** and **9b)** in a ratio 2:1, respectively; 47%; **9a**: ^1H NMR ($CDCl_3$) taken for the mixture: 1.30, 1.46 (2s, 6H, isopr.), 2.46 (s, 3H, tosyl), 2.88 (dd, 1H, *J* 1.5, 15.3 Hz, H-3'a), 3.11 (ddd, 1H, *J* 3.3, 4.0, 15.3 Hz, H-3'b), 4.09 (d, 1H, $J_{3,4}$ 3.3 Hz, H-3), 4.11 (dd, 1H, $J_{4,5}$ 5.1, $J_{5a,5b}$ 9.6 Hz, H-5a), 4.24 (dd, 1H, $J_{4,5b}$ 8.1 Hz, H-5b), 4.39 (ddd, 1H, H-4), 4.53 (d, 1H, $J_{1,2}$ 3.7 Hz, H-2), 5.21 (dd, 1H, *J* 1.5, 4.0 Hz, H-4'), 5.87 (d, 1H, H-1).

9b: ^1H NMR ($CDCl_3$) taken for the mixture: 1.31, 1.47 (2s, 6H, isopr.), 2.82 (dd, 1H, *J* 1.3, 15.0 Hz, H-3'a), 3.16 (ddd, 1H, *J* 2.9, 3.9, 15.0 Hz, H-3'b), 4.06 (d, 1H, $J_{3,4}$ 3.2 Hz, H-3), 4.11 (dd, 1H, H-5b), 4.26 (dd, 1H, $J_{4,5b}$ 8.2, $J_{5a,5b}$ 9.7 Hz, H-5b), 4.40 (ddd, 1H, H-4), 4.51 (d, 1H, $J_{1,2}$ 3.6 Hz, H-2), 5.17 (dd, 1H, *J* 1.3, 1.9 Hz, H-4'), 5.86 (d, 1H, H-1).

(4'R) 3-*O*-(azetidin-2-onyl-4')-1,2-*O*-isopropylidene-5-*O*-tosyl-α-D-xylofuranose (9a) from **15**. Compound **15** (0.066 g, 0.13 mmol) dissolved in pyridine (1 ml) and methylene chloride (1 ml) was treated with commercial HF/pyridine complex (0.2 mmol). After 5 min tosyl chloride (0.076 g, 0.4 mmol) was added and the mixture was left overnight at room temperature. Subsequently the mixture was poured into water and extracted with methylene chloride. The extract was washed with 5% sulfuric acid, saturated solution of sodium bicarbonate and water. The solution was dried, and evaporated. Crude **9a** was purified on a silica gel column using *t*-butyl methyl ether as an eluent to afford 0.022 g (54%); $[\alpha]_D$ -24.5 (*c* 0.3, CH_2Cl_2); MS (EI, HR) m/z: M^+ calcd for $C_{18}H_{23}NO_8S$: 413.11444. Found: 413.11449.

(4'R) and **(4'S) 3-*O*-(azetidin-2'-onyl-4')-1,2-*O*-isopropylidene-5-*O*-triisopropylbenzenesulfonyl-α-D-xylofuranose (12a** and **12b)**: in a ratio 3.3:1, respectively; 25%;

12a: ^1H NMR ($CDCl_3$) selective signals taken for the mixture: 2.96 (dd, 1H, *J* 1.5, 15.3 Hz, H-3'a), 3.17 (ddd,

1H, *J* 3.3, 4.0, 15.3, H-3'b), 4.15 (d, 1H, $J_{3,4}$ 3.2 Hz, H-3), 4.34 (dd, 1H, $J_{4,5b}$ 8.0, J_{5a5b} 9.7 Hz, H-5b), 4.56 (d, 1H, $J_{2,3}$ 3.70 Hz, H-2), 5.29 (dd, 1H, *J* 1.5, 4.0 Hz, H-4'), 5.89 (d, 1H, H-1), 6.45 (bs, 1H, NH).

12b: ^{1}H NMR ($CDCl_3$) selective signals taken for the mixture; 2.89 (dd, 1H, *J* 1.4, 15.0 Hz, H-3'a), 3.19 (ddd, 1H, *J* 2.9, 3.9, 15.0 Hz, H-3'b), 4.53 (d, 1H, $J_{1,2}$ 3.7 Hz, H-2), 5.21 (dd, 1H, *J* 1.4, 3.9 Hz, H-4'), 5.89 (d, 1H, H-1), 6.58 (bs, 1H, NH); MS (ET, HR) taken for the mixture **12a** and **12b**, m/z: $M^{+\cdot}$ calcd for $C_{26}H_{35}NO_8S$: 525.23963. Found: 525.2396.

(4'R) 3-*O*-(azetidin-2'-onyl-4')-1,2-*O*-isopropylidene-5-*O*-triphenylsilyl-α-D-xylofuranose (15): mp. 135-136°C; $[\alpha]_D$ -25.6° (*c* 1, CH_2Cl_2); IR ($CHCl_3$): 1780 cm^{-1}; ^{1}H NMR ($CDCl_3$): 1.30, 1.47 (2s, 6H, isopr.), 2.77 (dd, 1H, *J* 1.5, 15.2 Hz, H-3'a), 2.85 (ddd, 1H, *J* 3.0, 3.9, 15.2 Hz, H-3'b), 3.94 (dd, 1H, $J_{4,5a}$ 8.9, $J_{5a,56}$ 9.8 Hz, H-5a), 4.04 (dd, 1H, $J_{4,5b}$ 4.8 Hz, H-5b), 4.10 (d, 1H, $J_{3,4}$ 3.2 Hz, H-3), 4.35 (m, 1H, H-4), 4.55 (d, 1H, $J_{1,2}$ 3.8 Hz, H-2), 5.11 (dd, 1H, *J* 1.5, 3.9 Hz, H-4'), 5.87 (d, 1H, H-1), 6.22 (bs, 1H, NH); MS (EI, HR) m/z: ($M^{+\cdot}$-CH_3) calcd for $C_{28}H_{28}NO_6Si$: 502.16859. Found: 502.16847.

(4'R) and (4'S) 3-*O*-(azetidin-2'-onyl-4')-1,2-*O*-isopropylidene-α-D-glucofuranose (18) and (19). The mixture **3** (0.12 g, 0.36 mmol) was dissolved in acetic acid (4 ml) and water (1 ml) and left overnight. Subsequently solvent was evaporated and crude product was separated on a silica gel column using CH_2Cl_2 - methanol 95:5 $^v/_v$ as an eluent to give **18** (0.052 g) and **19** (0.014 g). **18**: mp. 167-168°C; $[\alpha]_D$ -5.7° (*c* 1, MeOH); IR (KBr): 3414, 3283, 3230, 1744 cm^{-1}; ^{1}H NMR (CH_3CN): 1.28, 1.44 (2s, 1.44 (2s, 6H, isopr.), 2.78 (dd, 1H, *J* 1.4, 15.0 Hz, H-3'a), 3.07 (ddd, 1H, *J* 3.0, 4.0, 15.0 Hz, H-3'b), 3.50 (dd, 1H, $J_{5.6a}$ 5.5, $J_{6a,6b}$ 11.6 Hz, H-6a), 3.66 (dd, 1H, *J* 2.9, 11.6 Hz, H-6b), 3.72 (m, 1H, H-5), 4.02 (dd, 1H, $J_{3,4}$ 2.9, $J_{4,5}$ 9.1 Hz, H-4), 4.06 (d, 1H, H-3), 4.60 (d, 1H, $J_{1,2}$ 3.7 Hz, H-2), 5.22 (dd, 1H, *J* 1.4, 4.0 Hz, H-4'), 5.81 (d, 1H, H-1); MS (EI, HR) m/z: (M^+-CH_3) calcd for $C_{11}H_{16}NO_7$: 274.09267. Found: 274.0926.

19: $[\alpha]_D$ -13.6° (*c* 0.14, MeOH); IR (CH_3): 1750 cm^{-1}; ^{1}H NMR (CH_3CN): 1.28, 1.44 (2s, 6H, isopr.), 2.77 (dd, 1H, *J* 1.4, 15.0 Hz, H-3'a), 3.07 (ddd, 1H, *J* 2.8, 4.0, 15.0 Hz, H-3'b), 3.51 (dd, 1H, $J_{5,6a}$ 5.6, $J_{6a,6b}$ 11.5 Hz, H-6a), 3.66 (dd, 1H, $J_{5,6b}$ 3.0 Hz, H-6b), 3.75 (m, 1H, H-5), 4.02 (dd, 1H, *J* 3.0, 9.0 Hz, H-4), 4.06 (d, 1H, H-3), 4.58 (d, 1H, $J_{1,2}$ 3.7 Hz, H-2), 5.23 (dd, 1H, *J* 1.4, 4.0 Hz, H-2), 5.81 (d, 1H, H-1). MS (EI, HR) m/z: (M^+-CH_3) calcd for $C_{11}H_{16}NO_7$: 274.09267. Found: 274.0926.

(4'R) and (4'S) 5-amino-5-deoxy-1,2-*O*-isopropylidene-3-*O*:5-*N*-(azetidin-2'-onyl-4')-α-D-xylofuranose (20 and 21). Compounds **9** (0.21 g, 0.5 mmol) was dissolved in acetonitrile (15 ml) and treated with tetrabutylammonium bromide (0.17 g, 0.5mmol) and pulverized anhydrous K_2CO_3 (0.7 g). The mixture was stirred and kept under reflux for 40 min. Subsequently toluene (10 ml) was added, the mixture was filtered, washed with water, dried, and evaporated. The crude product was separated on a silica gel column using ethyl acetate - hexane 1:1 $^v/_v$ as an eluent to give **20** (0.066 g, 55%) and **21** (0.043 g, 35%).

20: mp. 161-165°C; $[\alpha]_D$ 121.1° (*c* 0.9, CH_2Cl_2); IR ($CHCl_3$): 1765 cm^{-1}; ^{1}H NMR ($CDCl_3$): 1.33, 1.50 (2s, 6H, isopr.), 2.75 (d, 1H, *J* 15.1 Hz, H-3'a), 3.15 (m, 1H, H-3'b), 3.53 (dt, 1H, H-5a), 3.79 (dd, 1H, $J_{4,5a}$ 4.4, $J_{5a,5b}$ 13.8 Hz, H-5b), 4.33 (dd, 1H, *J* 0.3, 3.2 Hz, H-3), 4.43 (m, 1H, H-4), 4.62 (d, 1H, $J_{1,2}$ 3.8 Hz, H-2), 4.98

(dd, 1H, *J* 0.7, 3.2 Hz, H-4'), 5.97 (d, 1H, H-1); MS (EI, HR) m/z: $M^{+\cdot}$ calcd for $C_{11}H_{15}NO_5$: 241.0949.

21: mp. 156-158°C; $[\alpha]_D$ -29.8° (*c* 0.8, CH_2Cl_2); IR ($CHCl_3$): 1771 cm^{-1}; ^1H NMR ($CDCl_3$): 1.32, 1.49 (2s, 6H, isopr.), 2.79 (d, 1H, *J* 14.9 Hz, H-3'a), 3.18 (ddd, 1H, *J* 1.9, 3.2, 14.9 Hz, H-3'b), 3.25 (ddd, 1H, *J* 1.9, 3.9, 15.0 Hz, H-5a), 4.06 (m, 1H, H-4), 4.07 (d, 1H, *J* 15.0 Hz, H-5b), 4.14 (m, 1H, H-3), 4.51 (d, 1H, $J_{1,2}$ 3.7 Hz, H-2), 4.86 (d, 1H, *J* 3.2 Hz, H-4'), 5.90 (d, 1H, H-1); MS (EI, HR) m/z: $M^{+\cdot}$ calcd for $C_{11}H_{15}NO_5$: 241.09502. Found: 241.0952.

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References

1. Kunz, H.; Rück, K. *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 336.
2. Brandänge, S.; Josephson, S.; Mörch, L.; Vallen, S. *Acta Chem. Scand.* B **1981**, *35*, 273; Kunz, H.; Mohr, J. *J. Chem. Soc. Chem. Commun.* **1988**, 1315; Duhamel, L.; Angiland, P.; Desmurs, J.R.; Valuot, J.Y. *Synlett*, **1991**, 807; Kunz, H.; Müller, B.; Schanzenbach, D. *Angew. Chem. Int. Ed. Eng.* **1987**, *26*, 267; Reissig, H.V.; *Angew. Chem. Int. Ed. Engl.* **1992**, 288; Arnold, T.; Orschel, B.; Reissig, H.V. *ibid.* **1992**, 1033; Kunz, H.; Pees, K.-J. *J. Chem. Soc. Perkin Trans. 1* **1989**, 1169; Hirao, A.; Mochizuki, H.; Nakahama, S.; Yamazaki, N. *J. Org. Chem.* **1979**, *44*, 1720; Hirao, A.; Itsuno, S.; Mochizuki, H.; Nakahama, S.; Yamazaki, N. *N. Bull. Chem. Soc. Jpn.* **1981**, *54*, 1424; Hirao, A.; Nakahama, S.; Mochizuki, H.; Itsuno, S.; Yamazaki, N. *J. Org. Chem.*, **1980**, *45*, 4231; Hirao, A.; Itsuno, S.; Owa, M.; Nagami, S.; Mochizuki, H.; Zoorov, H.H.A.; Nakahama, S.; Yamazaki, N. *J. Chem. Soc. Perkin Trans 1* **1981**, 900; Duthaler, R.O.; Herold, P.; Wyler-Helfer, S.; Riediker, M. *Helv. Chim. Acta* **1990**, *93*, 659; Duhamel, P.; Eddine, J.J.; Valnot, J.-Y. *Tetrahedron Lett.*, **1987**, *28*, 3801; Lera, J.M.; Fernandez, J.; Aleudia, F. *Tetrahedron Lett.*, **1991**, *32*, 7299.
3. Kałuża, Z.; Wang Fudong; Bełżecki, C.; Chmielewski, M. *Tetrahedron Lett.*, **1989**, *30*, 5171.
4. Kałuża, Z.; Abramski, W.; Bełżecki, C.; Grodner, J.; Mostowicz, D.; Urbański, R.; Chmielewski, M. *Synlett*, **1994**, 539.
5. Bernardo, S.D.; Fengi, J.P.; Sasso, G.J.; Weigele, M. *J. Org. Chem.*, **1985**, *50*, 3457; Miller, J.C.; Toom, V.; Preuss, D.L; Blount, J.F.; Weigle, M. *J. Antibiot.* **1982**, *36*, 217; Hoppe, D.; Hilpert, T. *Tetrahedron*, **1987**, *43*, 2467.
6. Watanabe, W.H.; Coulon, L.E. *J. Am. Chem.Soc.*, **1957**, *57*, 2828.
7. Hungerbühler, E.; Biollaz, M.; Ernest, F.; Kalvoda, J.; Lang, M.; Schneider, P.; Sedelmaier. G. in "New Aspects of Organic Chemistry" I, Yoshida, Z.; Shiba, T.; Ohshiro, Y. (Eds), VCh, Weinheim, New York, **1989**, p.419.
8. Kałuża, Z.; Furman, B.; Urbańczyk-Lipkowska, Z. unpublished results.

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