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Creation of quarternary stereocentres via [3,3]-sigmatropic rearrangement of allylic thiocyanates. A synthetic approach to (+)-myriocin

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Abstract—A stereoselective approach to the advanced precursor of (+)-myriocin, 3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-methoxycarbonylamino-α-D-glucofuranose 3-*C*-carboxylic acid, via the [3,3]-sigmatropic rearrangement of allylic thiocyanates prepared from D-glucose is presented. From the observed results, supported by DFT calculations, we can conclude that the [3,3]-sigmatropic rearrangement of the thiocyanato group in allylic hexofuranosides is strongly influenced by the steric interaction of the 1,2-*O*-isopropylidene group in the transition states.

1. Introduction

[3,3]-Sigmatropic rearrangements when used as a tool for the formation of carbon–nitrogen bonds have an enormous potential for the synthesis of molecules containing nitrogen-bearing stereocentres. The prototype of this reaction is the Overman rearrangement which provides protected allylic amines with excellent stereocontrol.[1] Stereodefined allylic amines are important building blocks used for the synthesis of highly functionalized enantiomerically pure amino acid derivatives and alkaloid natural products.[2] We have recently reported thermally driven [3,3]-sigmatropic rearrangements of allylic thiocyanates and trichloroacetimidates as a way to synthesize protected allylic amines of varying structure.[3] As a continuation of our research, we herein report an extension of this methodology to sugar allylic thiocyanates and illustrate its potential for the stereocontrolled synthesis of the branched-chain amino sugar 3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-methoxycarbonylamino-α-D-glucofuranose 3-*C*-carboxylic acid **10** as an advanced intermediate for the synthesis of (+)-myriocin[4] and sphingofungins.[5]

2. Results and discussion

2.1. Experimental

The substrates for the aza-Claisen rearrangements were thiocyanates (*Z*)-**3** and (*E*)-**6** prepared from 3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranoses,[6] (*Z*)-**1** and (*E*)-**5** (Scheme 1). The starting thiocyanates (*Z*)-**3** and (*E*)-**6** were prepared by S_N2 displacement of the *O*-mesyl group in the corresponding mesylates, derived from allylic alcohols (*Z*)-**1** and (*E*)-**5**, by the thiocyanate group (KSCN/CH_3CN) (Scheme 1). In order to determine the best reaction conditions, a series of thermal and microwave induced rearrangements were performed. The thermal rearrangements of thiocyanates (*Z*)-**3** and (*E*)-**6**, which were carried out at 90 °C in *o*-xylene under N_2 for 4 h, afforded crystalline isothiocyanate **4**, as the sole reaction product in 85% and 88% yields after silica-gel chromatography. The microwave induced rearrangement of (*Z*)-**3** and (*E*)-**6** afforded isothiocyanate **4** in 83% and 88% yields (90 °C, heptane), within 2 h. The reaction was performed in closed vessels in a focused microwave reactor (CEM Discover), with control of the power and temperature by an infrared sensor. The diastereoisomeric isothiocyanate **4a** was not detected in any experiment.

Although the stereochemistry of the new quarternary carbon centre (C-3) introduced in **4** could not be established

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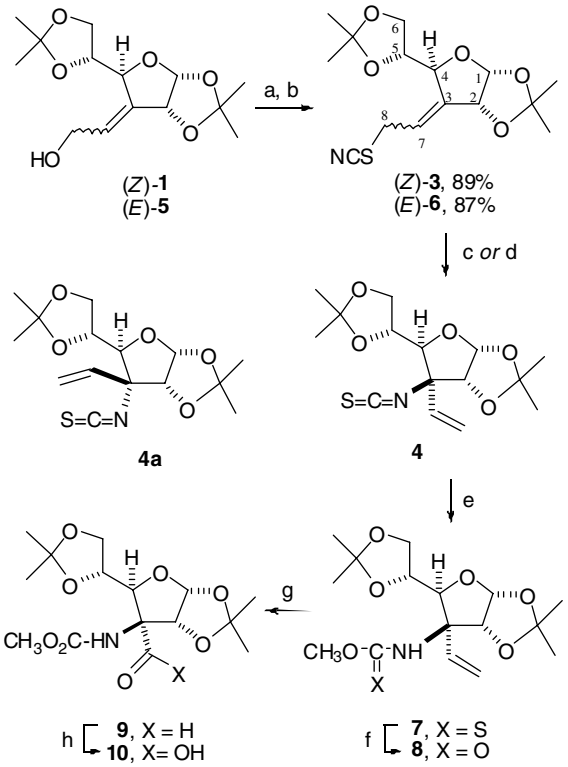
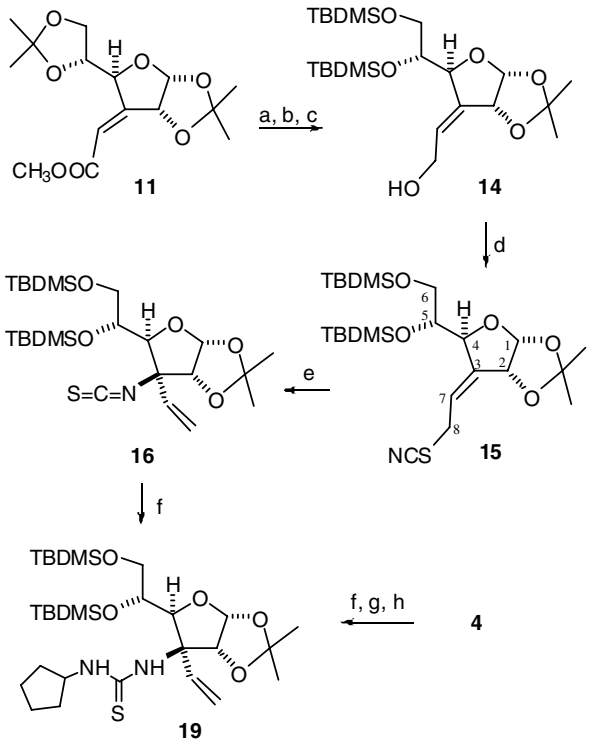


Scheme 1. Reagents and conditions: (a) MsCl, NEt_3; (b) KSCN, MeCN, (*Z*)-**3**, 83%, (*E*)-**6**, 86%, two steps; (c) Δ, *o*-xylene, 4 h, 90 °C, 85% from (*Z*)-**3**, 88% from (*E*)-**6**; (d) MW, heptane, 2 h, 83% from (*Z*)-**3**, 88% from (*E*)-**6**; (e) CH_3ONa, CH_3OH, 87%; (f) MNO, 88%; (g) $RuCl_3$, $NaIO_4$, 78%; (h) $NaClO_2$, 85%.

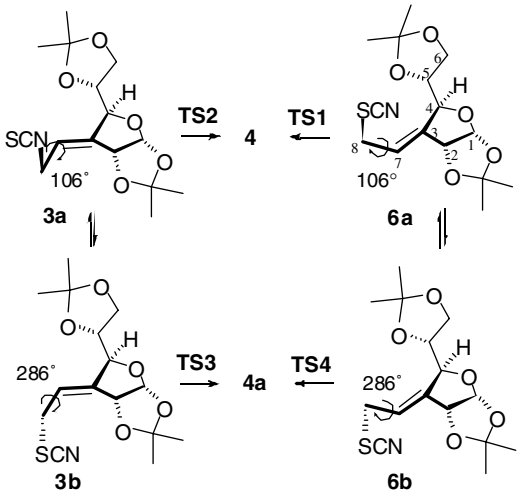


Scheme 2. Reagents and conditions: (a) Amberlite IR 120H, **12**, 84%; (b) TBDMSCl, im/DMF, **13**, 89%; (c) DIBAlH, CH_2Cl_2, 87%; (d) MsCl, NEt_3, KSCN, MeCN, 78%; (e) *o*-xylene, 90 °C, 6 h, 84%; (f) cyclopentyl amine, **17**, 89%; (g) CSA, MeOH, **18**, 84%; (h) TBDMSCl, im/DMF, 83%.

by its NMR spectroscopic analysis, it was determined by the X-ray analysis to be (*S*).[7] Isothiocyanate **4** was then converted to protected α-amino acid **10**, the desired precursor for the synthesis of myriocin. The reaction of **4** with CH_3ONa in methanol (1.44 mmol) at room temperature for 5 h gave thiouretane **7** in near quantitative yield. The treatment of **7** with mesitylnitrile oxide in acetonitrile afforded urethane **8** in 88% yield. The oxidation of **8** with $RuCl_3/NaIO_4$ ($CH_3CN/CCl_4/H_2O = 2/2/3$) gave aldehyde **9**. The treatment of **9** with $NaClO_2$ at 0 °C over 45 min led to amino acid **10** in 85% yield.

Although the decisive factor for the stereoselective outcome of the rearrangement seems to be the 1,2-*O*-isopropylidene group, an assumption that the large substituent at C-4 in the furanose ring might participate in the stereoselectivity cannot be excluded. To clarify this possibility, the rearrangement of thiocyanate **15** (Scheme 2) was investigated next. Thiocyanate **15** with large 5,6-di-*O*-(*t*-butyldimethyl)silyl protecting groups was prepared from the known[6] (*Z*)-α,β-unsaturated ester **11** by a series of functional group manipulations: (i) the selective removal of the 5,6-*O*-isopropylidene group with Amberlite IR 120H ($CH_3OH/H_2O = 9/1$, **12**, 84%); (ii) the 5,6-O-silylation of the resulting 5,6-diol **12** with TBDMSCl/imidazole in DMF at 70 °C (**13**, 89%); (iii) the DIBAl-H reduction of **13** in CH_2Cl_2 (**14**, 87%); and (iv) the mesylation of the resulting allylic alcohol **14** with MsCl/NEt_3 in CH_2Cl_2, and displacement of the *O*-mesyl group by the thiocyanate group by KSCN in MeCN (**15**, 78% both steps) (Scheme 2).

Finally, the rearrangement of **15** was performed under the same conditions as for **3** and **6** (90 °C, *o*-xylene, N_2, 6 h) and isothiocyanate **16** was isolated as the sole product in 84% yield. The absolute configuration at C-3 in **16** was unambiguously determined by chemical transformations (Scheme 3). Thus, the reaction of isothiocyanate **16** with cyclopentylamine led to thiourea **19** in 89% yield. This compound is in all respects identical to thiourea **19**, which



Scheme 3.

was prepared from **4** as follows: isothiocyanate **4** was converted to thiourea **17** in 89% yield after the addition of cyclopentylamine. Treatment of **17** with 10-camphorsulfonic acid (CSA) in CH_3OH afforded unprotected thiourea **18** in 84% yield. The subsequent reaction of **18** with TBDMSCl/imidazole in DMF at 70 °C gave **19**. Surprisingly, the absolute configuration at C-3 in **16** is the same as in **4.**

2.2. Theoretical

The purpose of the theoretical contribution of this work is to rationalize the observed high stereoselectivity of the rearrangement. In order to obtain reliable results, high-level density functional theory (DFT) which include electron correlation effects, were carried out. The Becke3LYP method was found to predict activation barriers for the pericyclic reactions in excellent agreement with the available experimental data.[8] The solvent effects have also been taken into account in this study, in order to obtain a more realistic model of the reaction.

The starting geometries for thiocyanates **3** and **6** was determined by a conformational search in which the torsional angle C3–C7–C8–S was varied as shown in Scheme 3. We found two pairs of stable conformers **3a**, **3b** and **6a**, **6b** with torsional angles 106° and 286°. These particular conformations result in a minimization of 1,3-allylic strain. Each transition structure was located using a QST3 routine implemented in the Gaussian 03 program.[14] The B3LYP/6-31G* geometry of the transition states **TS1**–**TS4** is given in Figure 1 along with the bond distances (in angstrom (Å)).

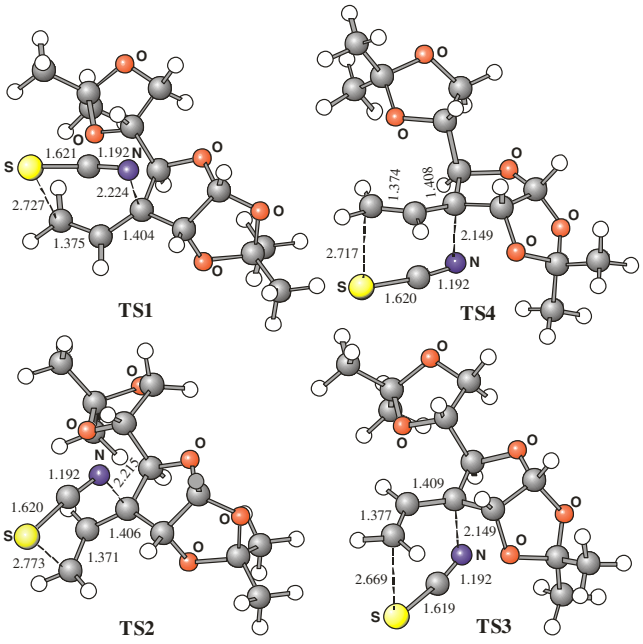


Figure 1. Optimized geometries (B3LYP/6-31G*) of the transition structures (**TS1**–**TS4**), bond distances (in angstrom (Å)).

From the calculations, for the pathway (**3a**→**TS2**→**4**) the activation energy ($\Delta E^{\ddagger}$) was found to be 7.52–7.68 kcal/mol lower than for the pathway (**3b**→**TS3**→**4a**). Analogously, for the pathway (**6a**→**TS1**→**4**) the activation energy ($\Delta E^{\ddagger}$) was found to be 7.71–7.69 kcal/mol lower than for the pathway (**6b**→**TS4**→**4a**) at the level of theory under study (Table 1). These large differences could be due to the steric hindrance between the rearranging thiocyanato and 1,2-*O*-isopropylidene groups as it appears from the geometry of **TS3** and **TS4** (Fig. 1). Therefore, the N–C bond formation occurred preferentially from the less hindered β-face of the furanose ring. This result is in agreement with the experimental data, since isothiocyanate **4a** was never observed in the reaction mixture.

Furthermore, the theoretical calculations of the solvent effect indicate that the stereoselectivity in toluene is quite similar to that in the gaseous phase. This result is in accordance with the literature data[15] showing that reaction rate of the rearrangement is reduced only in polar solvents.

3. Conclusion

From the observed results, supported by DFT calculations, we can conclude that the [3,3]-sigmatropic rearrangement of the thiocyanato group in allylic hexofuranosides **3**, **6** and **15** is strongly influenced by the steric interaction of the 1,2-*O*-isopropylidene group in the transition states. Thus, easy access to 3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-methoxycarbonylamino-α-D-glucofuranose 3-*C*-carboxylic acid **10**, make this compound an attractive key intermediate for the preparation of (+)-myriocin and sphingofungins. Applications directed towards the synthesis of enantiomerically pure non-proteinogenic amino acids are currently underway in our laboratory.

4. Experimental

4.1. General

Melting points were determined on a Kofler block and are uncorrected. Optical rotations were measured with a P3002 Krüss polarimeter in chloroform and reported as follows: $[\alpha]_D^{25}$ (*c* in g per 100 ml, solvent). NMR spectra were recorded at room temperature on a FT NMR spectrometer Varian Mercury Plus 400 (^{1}H at 400.13 MHz and ^{13}C at 100.6 MHz) and on a FT NMR spectrometer Varian UNITY-500 (^{1}H at 499.8 MHz and ^{13}C at 125.7 MHz) in $CDCl_3$. Chemical shifts are referenced either to tetramethylsilane as the internal standard for ^{1}H or to the solvent signal (^{13}C NMR, δ $CDCl_3 = 77.0$). Chemical shifts (in ppm) and coupling constants (in hertz) were obtained by first-order analysis. ^{13}C NMR multiplicities were determined using a DEPT pulse sequence. IR spectra were recorded on a Perkin–Elmer 599 IR spectrometer in $CHCl_3$; absorptions in cm^{-1}. The reaction course was routinely monitored by TLC (Merck 60 F_{254}) and the products were visualized by UV light absorption at 254 nm or by spraying with Mo-reagent or $KMnO_4$-reagent. All reactions were performed under an atmosphere of nitrogen when anhydrous solvents were used. Column chromatography was carried out on glass columns using silica gel

Table 1. Activation energies ($\Delta E^{\ddagger}$) of [3,3]-sigmatropic rearrangements for the pathways (**3a**→**TS2**→**4**), (**3b**→**TS3**→**4a**), (**7a**→**TS1**→**4**) and (**7b**→**TS4**→**4a**)

Pathway	Level of theory		$\Delta E^{\ddagger}$ (298 K)
3a→**TS2**→**4**	B3LYP/6-311+G**[a]	Gas phase	17.87
	B3LYP/6-311+G**[b]	Toluene	19.08
3b→**TS3**→**4a**	B3LYP/6-311+G**[a]	Gas phase	25.62
	B3LYP/6-311+G**[b]	Toluene	26.60
6a→**TS1**→**4**	B3LYP/6-311+G**[a]	Gas phase	18.82
	B3LYP/6-311+G**[b]	Toluene	19.84
6b→**TS4**→**4a**	B3LYP/6-311+G**[a]	Gas phase	26.51
	B3LYP/6-311+G**[b]	Toluene	27.01

[a] Energies at B3LYP/6-311+G**//B3LYP/6-31G* + ZPE at B3LYP/6-31G*.
[b] Energies at B3LYP/6-311+G**//B3LYP/6-31G* (SCRF (pcm), $\varepsilon = 2.379$, toluene) + ZPE at B3LYP/6-31G* gas phase.

Kieselgel (0.035–0.070 mm). Microwave experiments were conducted using a focused microwave system (CEM Discover). Reactions were performed in a glass vessel (10 ml) sealed with a septum. The temperature content of the vessel was monitored using a calibrated infrared sensor mounted under the vessel. All the experiments were performed using the stirring option. In all the experiments, a target temperature of 90 °C was selected together with a microwave power of 150 W. At the end of the reaction the vessel and contents were cooled rapidly using a stream of compressed air.

4.2. General procedure for the preparation of thiocyanates 3, 6 and 15

To a solution of allylic alcohol **1**, **5** or **14** (4.19 mmol) in dry CH_2Cl_2 (15 ml) were added Et_3N (0.87 ml, 6.29 mmol) and CH_3SO_2Cl (0.39 ml, 5.03 mmol) at 0 °C. The reaction mixture was stirred for 15 min at 0 °C and then for 1.5 h at room temperature. The solvent was evaporated under reduced pressure. The resulting residue was diluted with diethyl ether (30 ml) and the solid was removed by filtration. The evaporation of the solvent at reduced pressure afforded the crude mesylate which was used in the next reaction directly without further purification. To a solution of crude mesylate in CH_3CN (12 ml), KSCN (0.35 g, 3.62 mmol) was added. After being stirred for 2 h at room temperature, the solvent was evaporated. The residue was diluted with diethyl ether (35 ml) and the solid was removed by filtration. Evaporation of the solvent at reduced pressure and chromatography of the residue (cyclohexane–ethyl acetate, 5:1) afforded the thiocyanates **3**, **6** and **15**.

4.2.1. 3-Deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-(*Z*)-(2-thiocyanatoethylidene)-α-D-glucofuranose, 3. Yield 83%; colourless oil; $[\alpha]_D^{25} = +140.5$ (*c* 0.11, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.37 (3H, br s, CH_3), 1.39 (3H, br s, CH_3), 1.45 (3H, br s, CH_3), 1.48 (3H, br s, CH_3), 3.63 (1H, ddd, $J_{8,8} = 13.1$ Hz, $J_{8,7} = 7.1$ Hz, $J_{8,4} = 1.6$ Hz, H_8), 3.96 (1H, dd, $J_{6,6} = 8.2$ Hz, $J_{6,5} = 5.0$ Hz, H_6), 3.99 (1H, dddd, $J_{8,8} = 13.1$ Hz, $J_{8,7} = 9.1$ Hz, $J_{8,CH_3} = 0.7$ Hz, $J_{8,CH_3} = 0.4$ Hz, H_8), 4.03 (1H, ddd, $J_{5,4} = 7.1$ Hz, $J_{6,5} = 6.1$ Hz, $J_{6,5} = 5.0$ Hz, H_5), 4.10 (1H, dd, $J_{6,6} = 8.2$ Hz, $J_{6,5} = 6.1$ Hz, H_6), 4.67 (1H, dddd, $J_{5,4} = 7.1$ Hz, $J_{7,4} = 2.0$ Hz, $J_{8,4} = 1.6$Hz, $J_{4,2} = 1.2$ Hz, H_4), 5.17 (1H, ddd, $J_{2,1} = 4.4$ Hz, $J_{7,2} = 1.8$ Hz, $J_{4,2} = 1.2$ Hz, H_2), 5.87 (1H, d, $J_{2,1} = 4.4$ Hz, H_1), 6.08 (1H, dddd, $J_{8,7} = 9.1$ Hz, $J_{8,7} = 7.1$ Hz, $J_{7,4} = 2.0$ Hz, $J_{7,2} = 1.8$ Hz, H_7); ^{13}C NMR (125 MHz, $CDCl_3$): δ 25.4, 26.7, 27.4, 27.5, 32.3, 66.9, 77.5, 78.4, 80.1, 105.0, 110.0, 111.6, 113.0, 120.9, 145.6. Anal. Calcd for $C_{15}H_{21}NO_5S$: C, 55.03; H, 6.47; N, 4.28; S, 9.79. Found: C, 55.13; H, 6.37; N, 4.17; S, 9.65.

4.2.2. 3-Deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-(*E*)-(2-thiocyanatoethylidene)-α-D-glucofuranose, 6. Yield 86%; white crystals; mp 54–55 °C; $[\alpha]_D^{25} = +69.2$ (*c* 0.24, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.35 (3H, s, CH_3), 1.41 (3H, s, CH_3), 1.46 (3H, s, CH_3), 1.47 (3H, s, CH_3), 3.83–3.89 (3H, m, $2 \times H_8$, H_5), 3.94 (1H, dd, $J_{6,6} = 8.9$ Hz, $J_{6,5} = 6.3$ Hz, H_6), 4.16 (1H, dd, $J_{6,6} = 8.9$, $J_{6,5} = 6.3$ Hz, H_6), 4.80 (1H, d, $J_{5,4} = 8.7$ Hz, H_4), 5.05 (1H, dd, $J_{2,1} = 4.4$ Hz, $J_{7,2} = 1.7$ Hz, H_2), 5.80 (1H, d, $J_{2,1} = 4.4$ Hz, H_1), 6.09 (1H, ddd, 1H, $J_{8,7} = 8.2$ Hz, $J_{8,7} = 6.5$ Hz, $J_{7,2} = 1.7$ Hz, H_7); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.2, 26.5, 27.7, 27.8, 33.1, 68.0, 77.1, 80.5, 81.8, 104.1, 110.2, 112.0, 113.4, 123.1, 144.9. Anal. Calcd for $C_{15}H_{21}NO_5S$: C, 55.03; H, 6.47; N, 4.28; S, 9.79. Found: C, 55.10; H, 6.40; N, 4.36; S, 9.81.

4.2.3. 5,6-Bis(*O*-*tert*-butyldimethylsilyl)-3-deoxy-1,2-*O*-isopropylidene-3-*C*-(*Z*)-(2-thiocyanatoethylidene)-α-D-glucofuranose, 15. Yield 78%; colourless oil; $[\alpha]_D^{25} = +86.2$ (*c* 0.13, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.07 (3H, s, CH_3), 0.07 (3H, s, CH_3), 0.08 (3H, s, CH_3), 0.10 (3H, s, CH_3), 0.87 (9H, s, $3 \times CH_3$), 0.90 (9H, s, $3 \times CH_3$), 1.42 (3H, br s, CH_3), 1.44 (3H, br s, CH_3), 3.49 (1H, dd, $J_{6,6} = 10.4$ Hz, $J_{6,5} = 9.2$ Hz, H_6), 3.57 (1H, dd, $J_{6,6} = 10.4$ Hz, $J_{6,5} = 5.6$ Hz, H_6), 3.78 (1H, dd, $J_{8,8} = 13.1$ Hz, $J_{8,7} = 7.6$ Hz, H_8), 3.84 (1H, ddd, $J_{6,5} = 9.2$ Hz, $J_{6,5} = 5.6$ Hz, $J_{5,4} = 2.7$ Hz, H_5), 4.02 (1H, dd, $J_{8,8} = 13.1$ Hz, $J_{8,7} = 8.3$ Hz, H_8), 5.03 (1H, dd, $J_{5,4} = 2.7$ Hz, $J_{7,4} = 1.9$ Hz, H_4), 5.14 (1H, ddt, $J_{2,1} = 4.8$ Hz, $J_{7,2} = 1.9$ Hz, H_2), 5.79 (1H, ddt, $J_{8,7} = 8.3$ Hz, $J_{8,7} = 7.6$ Hz, $J_{7,4} = 1.9$ Hz, $J_{7,2} = 1.9$ Hz, H_7), 5.92 (1H, d, $J_{2,1} = 4.8$ Hz, H_1); ^{13}C NMR (100 MHz, $CDCl_3$): δ −5.5, −5.4, −4.6 ($2 \times C$), 17.9, 18.2, 25.8 ($3 \times C$), 26.0 ($3 \times C$), 26.7, 27.8, 32.5, 62.8, 74.7, 79.8, 83.1, 105.7, 111.9, 113.0, 120.0, 144.9. Anal. Calcd for $C_{24}H_{45}NO_5SSi_2$: C, 55.88; H, 8.79; N, 2.72; S, 6.22. Found: C, 55.75; H, 8.87; N, 2.53; S, 6.33.

4.3. 3-Deoxy-1,2:5,6-di-*O*-isopropylidene-3-isothiocyanato-3-*C*-vinyl-α-D-glucofuranose, 4

Microwave-assisted synthesis of **4**: (*Z*)-Thiocyanate **3** (0.30 g, 0.98 mmol) was weighed in a 10 ml glass pressure

microwave tube equipped with a magnetic stirrer bar. Heptane (5 ml) was added, the tube was closed with a silicon septum and the reaction mixture was subjected to microwave irradiation for 2 h (power: 150 W, temperature: 90 °C, pressure: 12 bar). The reaction mixture was allowed to cool to room temperature and transferred to a round bottom flask. The solvent was evaporated under reduced pressure, and the chromatography of the residue on silica gel (cyclohexane–ethyl acetate, 7:1) afforded 0.26 g (83%) of isothiocyanate **4**. (*E*)-Thiocyanate **6** gave at identical conditions, isothiocyanate **4** in 88% yield. *Conventional method for the synthesis of* **4**: A solution of (*Z*)-thiocyanate **3** (0.75 g, 2.29 mmol) in dry *o*-xylene (15 ml) was heated at 90 °C for 4 h under a nitrogen atmosphere. The solvent was evaporated under reduced pressure. The chromatography of the residue on silica gel (cyclohexane–ethyl acetate, 7:1) afforded 0.64 g (85%) of isothiocyanate **4**. A solution of (*E*)-thiocyanate **6** (0.61 g, 1.86 mmol) in dry *o*-xylene (12 ml) was heated at 90 °C for 4 h under a nitrogen atmosphere. The solvent was evaporated under reduced pressure, and the chromatography of the residue on silica gel (cyclohexane–ethyl acetate, 7:1) afforded 0.54 g (88%) of isothiocyanate **4**; white crystals; mp 81–83 °C; $[\alpha]_D^{25} = +51.1$ (*c* 0.23, $CHCl_3$); IR ($CHCl_3$): 2040 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.33 (6H, s, $2 \times CH_3$), 1.39 (3H, s, CH_3), 1.55 (3H, s, CH_3), 4.08 (1H, dd, $J_{6,6} = 8.6$ Hz, $J_{6,5} = 5.4$ Hz, H_6), 4.10 (1H, d, $J_{5,4} = 6.6$ Hz, H_4), 4.11 (1H, dd, $J_{6,6} = 8.6$ Hz, $J_{6,5} = 6.2$ Hz, H_6), 4.22 (1H, ddd, $J_{5,4} = 6.6$ Hz, $J_{6,5} = 6.2$ Hz, $J_{6,5} = 5.4$ Hz, H_5), 4.52 (1H, d, $J_{2,1} = 3.5$ Hz, H_2), 5.41 (1H, d, $J_{8cis,7} = 10.6$ Hz, H_{8cis}), 5.60 (1H, d, $J_{8trans,7} = 17.0$ Hz, H_{8trans}), 5.93 (1H, dd, $J_{8trans,7} = 17.0$ Hz, $J_{8cis,7} = 10.6$ Hz, H_7), 5.95 (1H, d, $J_{2,1} = 3.5$ Hz, H_1); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.2, 26.5, 26.7, 26.7, 66.6, 73.3, 75.1, 82.3, 88.2, 104.4, 109.6, 113.4, 118.2, 130.7, 138.9. Anal. Calcd for $C_{15}H_{21}NO_5S$: C, 55.03; H, 6.47; N, 4.28; S, 9.79. Found: C, 55.19; H, 6.31; N, 4.30; S, 9.82.

4.3.1. 3-Deoxy-1,2:5,6-di-*O*-isopropylidene-3-methoxythiocarbonylamino-3-*C*-vinyl-α-D-glucofuranose, 7. To a solution of sodium methoxide (0.078 g, 1.44 mmol) in dry methanol (13 ml) was added isothiocyanate **4** (0.43 g, 1.31 mmol). The reaction mixture was stirred at room temperature for 5 h under a nitrogen atmosphere. The solvent was evaporated under reduced pressure and the residue partitioned between CH_2Cl_2 (15 ml) and water (5 ml). The organic layer was dried over Na_2SO_4 and the solvent evaporated under reduced pressure. The chromatography of the residue (cyclohexane–ethyl acetate, 5:1) afforded 0.41 g (87%) of compound **7** as a colourless oil; $[\alpha]_D^{25} = +16.3$ (*c* 0.18, $CHCl_3$); ^1H NMR (400 MHz, CD_3COCD_3): δ 1.31 (3H, s, CH_3), 1.32 (3H, s, CH_3), 1.49 (3H, s, CH_3), 1.52 (3H, s, CH_3), 3.97 (3H, s, CH_3O), 4.00–4.06 (2H, m, $2 \times H_6$), 4.15 (1H, d, $J_{5,4} = 3.3$ Hz, H_4), 4.64 (1H, ddd, $J_{6,5} = 7.1$ Hz, $J_{6,5} = 7.1$ Hz, $J_{5,4} = 3.3$ Hz, H_5), 5.00 (1H, d, $J_{2,1} = 3.6$ Hz, H_2), 5.28 (1H, d, $J_{8trans,7} = 17.6$ Hz, H_{7trans}), 5.31 (1H, d, $J_{8cis,7} = 11.1$ Hz, H_{8trans}), 5.88 (1H, d, $J_{2,1} = 3.6$ Hz, H_1), 6.05 (1H, dd, $J_{8trans,7} = 17.6$ Hz, $J_{8cis,7} = 11.1$ Hz, H_7), 8.75 (1H, br s, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.8, 26.4 (2 × C), 26.7, 58.2, 65.7, 71.3, 74.8, 79.2, 85.0, 104.0, 110.6, 112.5, 117.9, 132.0, 192.0. Anal. Calcd for $C_{16}H_{25}NO_6S$: C, 53.47; H, 7.01; N, 3.90; S, 8.92. Found: C, 53.32; H, 7.10; N, 3.83; S, 8.79.

4.3.2. 3-Deoxy-1,2:5,6-di-*O*-isopropylidene-3-methoxycarbonylamino-3-*C*-vinyl-α-D-glucofuranose, 8. To a solution of **7** (0.32 g, 0.89 mmol) in CH_3CN (9 ml) was added mesitylnitrile oxide (0.158 g, 0.98 mmol). The reaction mixture was stirred at room temperature for 4 h, acetonitrile was evaporated under reduce pressure. Chromatography of the residue on silica gel (cyclohexane–ethyl acetate, 3:1) gave 0.27 g (88%) of **8** as a colourless oil; $[\alpha]_D^{25} = +31.4$ (*c* 0.26, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 1.33 (3H, s, CH_3), 1.35 (3H, s, CH_3), 1.46 (3H, s, CH_3), 1.55 (3H, s, CH_3), 3.66 (1H, s, CH_3O), 4.03–4.09 (3H, m, $2 \times H_6$, H_5), 4.42 (1H, m, H_4), 5.23 (1H, br d, $J_{2,1} = 3.5$ Hz, H_2), 5.36 (1H, dd, $J_{7cis,6} = 10.9$ Hz, $J_{7cis,7trans} = 0.6$ Hz, H_{7cis}), 5.37 (1H, dd, $J_{7trans,6} = 17.5$ Hz, $J_{7cis,7trans} = 0.6$ Hz, H_{7trans}), 5.93 (1H, d, $J_{2,1} = 3.5$ Hz, H_1), 6.04 (1H, dd, $J_{7trans,6} = 17.5$ Hz, $J_{7cis,6} = 10.9$ Hz, H_6), 6.32 (1H, br s, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.9, 26.2, 26.3, 26.8, 52.1, 66.0, 68.2, 74.8, 79.9, 84.8, 104.4, 110.1, 112.1, 116.9, 133.3, 155.9. Anal. Calcd for $C_{16}H_{25}NO_7$: C, 55.97; H, 7.34; N, 4.08. Found: C, 55.75; H, 7.47; N, 4.16.

4.3.3. 3-Deoxy-1,2:5,6-di-*O*-isopropylidene-3-methoxycarbonylamino-α-D-glucopyranose 3-*C*-carbaldehyde, 9. To a solution of **8** (0.22 g, 0.64 mmol) in $CCl_4/CH_3CN/H_2O$ (7 ml, 2/2/3) were added sodium periodate (0.56 g, 2.63 mmol) and ruthenium trichloride hydrate (3.5 mg, 2.5 mol %). The reaction mixture was stirred at room temperature for 1.5 h, then extracted with CH_2Cl_2 (3×20 ml). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by chromatography on silica gel (cyclohexane–ethyl acetate, 3:1) to afford 0.18 g (78%) of compound **9** as a colourless oil; $[\alpha]_D^{25} = +46.3$ (*c* 0.16, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 1.27 (3H, s, CH_3), 1.32 (3H, s, CH_3), 1.33 (3H, s, CH_3), 1.61 (3H, s, CH_3), 3.69 (3H, s, CH_3O), 4.02–4.13 (3H, m, $2 \times H_6$, H_5), 4.52 (1H, d, $J_{5,4} = 8.0$ Hz, H_4), 5.18 (1H, d, $J_{2,1} = 3.5$ Hz, H_2), 5.80 (1H, br s, NH), 6.19 (1H, d, $J_{2,1} = 3.5$ Hz, H_1), 9.65 (1H, s, CHO); ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.8, 25.9, 26.6, 26.8, 52.5, 67.1, 71.2, 73.1, 80.9, 87.0, 107.2, 109.9, 113.0, 155.9, 195.4. Anal. Calcd for $C_{15}H_{23}NO_8$: C, 52.17; H, 6.71; N, 4.06. Found: C, 52.01; H, 6.41; N, 4.18.

4.3.4. 3-Deoxy-1,2:5,6-di-*O*-isopropylidene-3-methoxycarbonylamino-α-D-glucofuranose 3-*C*-carboxylic acid, 10. A solution of $NaClO_2$ (0.30 g, 3.35 mmol) and NaH_2PO_4 (0.376 g, 2.41 mmol) in 2 ml of water was added dropwise to a solution of aldehyde **9** (0.125 g, 0.36 mmol) in 8.2 ml acetonitrile/*tert*-butylalcohol/2-methyl-2-butene (4/4/1) at 0 °C over 5 min and then stirred at the same temperature for 45 min. The reaction mixture was poured into brine (10 ml) and extracted with ethyl acetate (2×25 ml). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by chromatography on silica gel (dichloromethane–methanol, 9:1) and afforded 0.112 g (85%) of carboxylic acid **10**;

white crystals; mp 95–97 °C; $[\alpha]_D^{25} = +86$ (*c* 0.195, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 1.34 (3H, s, CH_3), 1.37 (3H, s, CH_3), 1.45 (3H, s, CH_3), 1.55 (3H, s, CH_3), 3.75 (3H, s, CH_3O), 3.96 (1H, dd, $J_{6,6} = 8.8$ Hz, $J_{6,5} = 7.4$ Hz, H_6), 4.10 (1H, dd, $J_{6,6} = 8.8$ Hz, $J_{6,5} = 6.5$ Hz, H_6), 4.51 (1H, ddd, $J_{6,5} = 7.4$ Hz, $J_{6,5} = 6.5$ Hz, $J_{4,3} = 4.7$ Hz, H_5), 4.76 (1H, d, $J_{4,3} = 4.7$ Hz, H_4), 5.10 (1H, d, $J_{2,1} = 3.9$ Hz, H_2), 6.01 (1H, d, $J_{2,1} = 3.9$ Hz, H_1), 7.05 (1H, br s, NH); ^{13}C NMR (125 MHz, $CDCl_3$): δ 25.1, 25.9, 26.3, 26.6, 53.3, 65.9, 70.3, 74.1, 79.2, 84.1, 104.6, 109.9, 113.1, 158.1, 169.1. Anal. Calcd for $C_{15}H_{23}NO_9$: C, 49.86; H, 6.42; N, 3.88. Found: C, 49.92; H, 6.34; N, 3.68.

4.3.5. 3-*C*-(*Z*)-Carbomethoxymethylene-3-deoxy-1,2-*O*-isopropylidene-α-D-glucofuranose, 12. To a solution of (*Z*)-α,β-unsaturated ester **11** (1.00 g, 3.18 mmol) in MeOH/water (10 ml, 9:1) was added Amberlite IR 120H resin (2 g). The mixture was stirred at room temperature for 24 h, filtered and the solid washed with MeOH (3 × 3 ml). Evaporation of the solvent from the combined filtrates gave an oil, which was purified by chromatography on silica gel (cyclohexane–ethyl acetate, 1:1) to afford 0.73 g (84%) of diol **12** as a colourless oil; $[\alpha]_D^{25} = +126.5$ (*c* 0.29, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 1.42 (3H, br s, CH_3), 1.50 (3H, br s, CH_3), 3.72 (1H, ddd, $J_{5,4} = 6.8$ Hz, $J_{6,5} = 5.0$ Hz, $J_{6,5} = 5.0$ Hz, H_5), 3.78 (3H, s, CH_3O), 3.79 (2H, m, H_6), 4.82 (1H, ddd, $J_{5,4} = 6.8$ Hz, $J_{7,4} = 2.2$ Hz, $J_{4,2} = 1.5$ Hz, H_4), 5.76 (1H, dt, $J_{2,1} = 4.2$ Hz, $J_{7,2} = 1.5$ Hz, $J_{4,2} = 1.5$ Hz, H_2), 5.88 (1H, d, $J_{2,1} = 4.2$ Hz, H_1), 5.93 (1H, dd, $J_{7,4} = 2.2$ Hz, $J_{7,2} = 1.5$ Hz, H_7); ^{13}C NMR (125 MHz, $CDCl_3$): δ 27.2, 27.3, 51.8, 63.4, 73.3, 78.3, 79.9, 104.8, 113.0, 117.1, 156.0, 165.5. Anal. Calcd for $C_{12}H_{18}O_7$: C, 52.55; H, 6.62. Found: C, 52.71; H, 6.46.

4.3.6. 5,6-Bis(*O*-*tert*-butyldimethylsilyl)-3-*C*-(*Z*)-carbomethoxymethylene-3-deoxy-1,2-*O*-isopropylidene-α-D-glucofuranose, 13. To a solution of diol **12** (0.70 g, 2.55 mmol) in DMF (5 ml) were added imidazole (0.74 g, 10.20 mmol), TBDMSCl (0.81 g, 5.36 mmol) and DMAP (78 mg, 0.64 mmol). The reaction mixture was stirred at 70 °C for 2.5 h. After dilution with ice water (15 ml), the solution was extracted with Et_2O (3 × 25 ml). The combined organic layers were dried (Na_2SO_4) and concentrated at reduced pressure. The residue was purified by chromatography on silica gel (cyclohexane–ethyl acetate, 11:1) to afford 1.15 g (89%) of **13** as a colourless oil; $[\alpha]_D^{25} = +93.8$ (*c* 0.25, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 0.05 (3H, s, CH_3), 0.06 (3H, s, CH_3), 0.07 (3H, s, CH_3), 0.08 (3H, s, CH_3), 0.86 (9H, s, 3 × CH_3), 0.88 (9H, s, 3 × CH_3), 1.44 (3H, br s, CH_3), 1.45 (3H, br s, CH_3), 3.54 (1H, dd, $J_{6,6} = 10.5$ Hz, $J_{6,5} = 8.3$ Hz, H_6), 3.60 (1H, dd, $J_{6,6} = 10.5$ Hz, $J_{6,5} = 5.4$ Hz, H_6), 3.78 (3H, s, CH_3O), 3.87 (1H, ddd, $J_{6,5} = 8.3$ Hz, $J_{6,5} = 5.4$ Hz, $J_{5,4} = 2.9$ Hz, H_5), 5.04 (1H, ddd, $J_{5,4} = 2.9$ Hz, $J_{7,4} = 1.9$ Hz, $J_{4,2} = 1.5$ Hz, H_4), 5.59 (1H, ddd, $J_{2,1} = 4.4$ Hz, $J_{7,2} = 1.8$ Hz, $J_{4,2} = 1.5$ Hz, H_2), 5.91 (1H, d, $J_{2,1} = 4.4$ Hz, H_1), 6.00 (1H, dd, $J_{7,4} = 1.9$ Hz, $J_{7,2} = 1.8$ Hz, H_7); ^{13}C NMR (125 MHz, $CDCl_3$): δ −5.5, −5.5, −4.7, −4.6, 17.9, 18.2, 25.8 (6 × C), 27.5, 27.6, 51.6, 63.1, 75.3, 79.7, 82.5, 105.5, 112.7, 116.6, 156.4, 165.4. Anal. Calcd for $C_{24}H_{46}O_7Si_2$: C, 57.33; H, 9.22. Found: C, 57.18; H, 9.36.

4.3.7. 5,6-Bis(*O*-*tert*-butyldimethylsilyl)-3-deoxy-3-*C*-(*Z*)-(2-hydroxyethylidene)-1,2-*O*-isopropylidene-α-D-glucofuranose, 14. To a solution of **13** (1.00 g, 1.99 mmol) in dry CH_2Cl_2 (9 ml) was added DIBAl-H (6 ml of 1.2 M toluene solution) at −10 °C. The reaction mixture was stirred at −10 °C for 40 min and then quenched with MeOH (1.5 ml). The mixture was allowed to warm to room temperature and poured into 30% aqueous K/Na-tartarate (30 ml). After being stirred for 30 min, the product was extracted with CH_2Cl_2 (3 × 30 ml). The combined organic layers were dried (Na_2SO_4) and the solvent was evaporated under reduced pressure. Chromatography of the residue (cyclohexane–ethyl acetate, 5:1) afforded 0.82 g (87%) of allylic alcohol **14** as a colourless oil; $[\alpha]_D^{25} = +67.3$ (*c* 0.13, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 0.05 (3H, s, CH_3), 0.05 (3H, s, CH_3), 0.07 (3H, s, CH_3), 0.10 (3H, s, CH_3), 0.86 (9H, s, 3 × CH_3), 0.88 (9H, 3 × CH_3), 3.47 (1H, dd, $J_{6,6} = 10.2$ Hz, $J_{6,5} = 5.6$ Hz, H_6), 3.53 (1H, dd, $J_{6,6} = 10.2$ Hz, $J_{6,5} = 8.9$ Hz, H_6), 3.80 (1H, ddd, $J_{6,5} = 8.9$ Hz, $J_{6,5} = 5.6$ Hz, $J_{5,4} = 2.6$ Hz, H_5), 4.39 (1H, ddd, $J_{8,7} = 6.6$ Hz, $J_{8,4} = 1.1$ Hz, $J_{8,2} = 1.1$ Hz, H_8), 4.28 (1H, ddd, $J_{8,7} = 5.5$ Hz, $J_{8,4} = 1.1$ Hz, $J_{8,2} = 1.1$ Hz, H_8), 4.99 (1H, m, H_4), 5.19 (1H, m, H_2), 5.93 (1H, d, $J_{2,1} = 4.8$ Hz, H_1), 6.00 (1H, ddd, $J_{7,4} = 2.0$ Hz, $J_{8,7} = 1.1$ Hz, $J_{8,7} = 1.1$ Hz, H_7); ^{13}C NMR (125 MHz, $CDCl_3$): δ −5.5, −5.4, −4.7, −4.6, 17.9, 18.2, 25.8 (6 × C), 27.7, 27.8, 60.5, 62.0, 75.0, 78.0, 83.4, 105.8, 112.6, 126.8, 140.2. Anal. Calcd for $C_{23}H_{46}O_6Si_2$: C, 58.18; H, 9.77. Found: C, 58.32; H, 9.55.

4.3.8. 5,6-Bis(*O*-*tert*-butyldimethylsilyl)-3-deoxy-1,2-*O*-isopropylidene-3-isothiocyanato-3-*C*-vinyl-α-D-glucofuranose, 16. A solution of (*Z*)-thiocyanate **15** (0.45 g, 0.87 mmol) in dry *o*-xylene (7 ml) was heated at 90 °C for 6 h under a nitrogen atmosphere. The solvent was evaporated at reduced pressure; chromatography of the residue on silica gel (cyclohexane–ethyl acetate, 15:1) afforded 0.38 g (84%) of isothiocyanate **16** as a colourless oil; $[\alpha]_D^{25} = +21.3$ (*c* 0.13, $CHCl_3$); IR ($CHCl_3$): 2048 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 0.05 (3H, s, CH_3), 0.06 (3H, s, CH_3), 0.07 (3H, s, CH_3), 0.09 (3H, s, CH_3), 0.87 (9H, s, 3 × CH_3), 0.90 (9H, s, 3 × CH_3), 1.31 (3H, br s, CH_3), 1.52 (3H, br s, CH_3), 3.72 (1H, dd, $J_{6,6} = 10.9$ Hz, $J_{6,5} = 3.1$ Hz, H_6), 3.74 (1H, dd, $J_{6,6} = 10.9$ Hz, $J_{6,5} = 3.1$ Hz, H_6), 3.88 (1H, dt, $J_{5,4} = 7.4$ Hz, $J_{6,5} = 3.1$ Hz, $J_{6,5} = 3.1$ Hz, H_5), 4.30 (1H, d, $J_{5,4} = 7.4$ Hz, H_4), 4.49 (1H, d, $J_{2,1} = 3.6$ Hz, H_2), 5.34 (1H, d, $J_{8cis,7} = 10.6$ Hz, H_{8cis}), 5.53 (1H, d, $J_{8trans,7} = 17.1$ Hz, H_{8trans}), 5.91 (1H, d, $J_{2,1} = 3.6$ Hz, H_1), 5.92 (1H, dd, $J_{8trans,7} = 17.1$ Hz, $J_{8cis,7} = 10.6$ Hz, H_7); ^{13}C NMR (100 MHz, $CDCl_3$): δ −5.5 (2 × C), −4.3, −4.1, 18.1, 18.3, 25.9 (3 × C), 26.0 (3 × C), 26.5, 26.6, 64.4, 72.0, 74.7, 81.0, 89.2, 103.6, 112.9, 117.0, 132.0, 137.0. Anal. Calcd for $C_{24}H_{45}NO_5SSi_2$: C, 55.88; H, 8.79; N, 2.72; S, 6.22. Found: C, 55.97; H, 8.64; N, 2.86; S, 6.05.

4.3.9. 3-Deoxy-3-(*N*-cyclopentylthiocarboxamido)-1,2:5,6-di-*O*-isopropylidene-3-*C*-vinyl-α-D-glucofuranose, 17. To a solution of isothiocyanate **4** (0.24 g, 0.73 mmol) in dry Et_2O (6 ml) was added cyclopentylamine (0.080 ml, 0.81 mmol). The reaction mixture was stirred at room tem-

perature for 1.5 h. The solvent was removed under reduced pressure and chromatography of the residue on silica gel (cyclohexane–ethyl acetate, 3:1) gave 0.27 g (89%) of pure thiourea **17** as a colourless oil; $[\alpha]_D^{25} = +77.1$ (*c* 0.27, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 1.32 (3H, br s, CH_3), 1.34 (3H, br s, CH_3), 1.43 (2H, m, CH_2), 1.46 (3H, br s, CH_3), 1.54 (3H, br s, CH_3), 1.63 (4H, m, CH_2), 2.05 (2H, m, CH_2), 4.03 (1H, d, $J_{5,4} = 8.1$ Hz, H_4), 4.07 (1H, dd, $J_{6,6} = 8.9$ Hz, $J_{6,5} = 4.9$ Hz, H_6), 4.13 (1H, dd, $J_{6,6} = 8.9$ Hz, $J_{6,5} = 6.3$ Hz, H_6), 4.24 (1H, ddd, $J_{5,4} = 8.1$ Hz, $J_{6,5} = 6.3$ Hz, $J_{6,4} = 4.9$ Hz, H_5), 4.56 (2H, m, H_2), 5.56 (1H, d, $J_{8cis,7} = 10.9$ Hz, H_{8cis}), 5.57 (1H, d, $J_{8trans,7} = 17.8$ Hz, H_{8trans}), 5.89 (1H, d, $J_{2,1} = 3.6$ Hz, H_1), 5.96 (1H, dd, $J_{8trans,7} = 17.8$ Hz, $J_{8cis,7} = 10.9$ Hz, H_7), 6.40 (1H, br s, NH), 6.58 (1H, br s, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.6, 23.7, 25.1, 26.3, 26.7 (2 × C), 32.2, 32.8, 58.0, 67.3, 68.9, 72.8, 81.6, 86.9, 103.6, 110.4, 113.0, 120.9, 131.0, 180.0. Anal. Calcd for $C_{20}H_{32}N_2O_5S$: C, 58.23; H, 7.82; N, 6.79; S, 7.77. Found: C, 58.04; H, 7.94; N, 6.64; S, 7.59.

4.3.10. 3-Deoxy-3-(*N*-cyclopentylthiocarboxamido)-1,2-*O*-isopropylidene-3-*C*-vinyl-α-D-glucofuranose, 18. To a solution of **17** (0.21 g, 0.51 mmol) in methanol (6 ml) was added 10-camphorsulfonic acid (29.5 mg, 0.127 mmol). The reaction mixture was heated at reflux for 4 h. The solvent was evaporated and the residue was partitioned between CH_2Cl_2 (14 ml) and saturated aqueous $NaHCO_3$ (4 ml). The organic layer was dried over Na_2SO_4 and the solvent evaporated under reduced pressure. Chromatography of the residue on silica gel (cyclohexane–ethyl acetate, 1:1) afforded 0.16 g (84%) of **18** as a colourless oil; $[\alpha]_D^{25} = +109.5$ (*c* 0.20, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 1.33 (3H, s, CH_3), 1.47 (2H, m, CH_2), 1.55 (3H, s, CH_3), 1.63 (4H, m, 2 × CH_2), 2.02 (2H, m, CH_2), 3.69 (1H, dd, $J_{6,6} = 11.6$ Hz, $J_{6,5} = 3.9$ Hz, H_6), 3.75 (1H, dd, $J_{6,6} = 11.6$ Hz, $J_{6,5} = 7.2$ Hz, H_6) 4.07 (1H, d, $J_{5,4} = 5.5$ Hz, H_4), 4.19 (1H, m, H_2), 4.45 (1H, m, H_5), 5.51 (1H, d, $J_{8trans,7} = 17.6$ Hz, H_{8trans}), 5.53 (1H, d, $J_{8cis,7} = 11.1$ Hz, H_{8cis}), 5.92 (1H, d, $J_{2,1} = 3.7$ Hz, H_1), 6.08 (1H, dd, $J_{8trans,7} = 17.6$ Hz, $J_{8cis,7} = 11.1$ Hz, H_7), 6.27 (1H, br s, NH), 7.56 (1H, m, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.6, 23.7, 26.3, 26.6, 32.8, 32.9, 57.7, 63.3, 65.9, 70.4, 80.5, 85.1, 104.0, 112.7, 120.4, 131.4, 180.0. Anal. Calcd for $C_{17}H_{28}N_2O_5S$: C, 54.82; H, 7.58; N, 7.52; S, 8.61. Found: C, 54.70; H, 7.61; N, 7.64; S, 8.50.

4.3.11. 5,6-Bis(*O*-*tert*-butyldimethylsilyl)-3-(*N*-cyclopentylthiocarboxamido)-3-deoxy-1,2-*O*-isopropylidene-3-*C*-vinyl-α-D-glucofuranose, 19. (i) To a solution of **18** (0.12 g, 0.32 mmol) in DMF (1 ml) were added imidazole (65.4 mg, 0.96 mmol), TBDMSCl (0.135 g, 0.896 mmol) and DMAP (39.1 mg, 0.32 mmol). The reaction mixture was heated at 65 °C for 6 h. The mixture was partitioned between diethyl ether (12 ml) and ice water (5 ml). The organic layer was dried (Na_2SO_4) and the solvent evaporated under reduced pressure. The chromatography of the residue (cyclohexane–ethyl acetate, 9:1) afforded 0.16 g (83%) of thiourea **19** as a colourless oil. (ii) To a solution of isothiocyanate **16** (0.21 g, 0.41 mmol) in dry Et_2O (6 ml) was added cyclopentylamine (0.044 ml, 0.45 mmol). The reaction mixture was stirred at room temperature for 1 h. The solvent was removed under reduced pressure and chromatography of the residue on silica gel (cyclohexane–ethyl acetate, 9:1) gave 0.22 g (89%) of thiourea **19** as a colourless oil; $[\alpha]_D^{25} = +97.5$ (*c* 0.25, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 0.00 (3H, s, CH_3), 0.01 (3H, s, CH_3), 0.14 (3H, s, CH_3), 0.22 (3H, s, CH_3), 0.86 (9H, s, 3 × CH_3), 0.96 (9H, s, 3 × CH_3), 1.32 (3H, s, CH_3), 1.43 (2H, m, CH_2), 1.54 (3H, s, CH_3), 1.62 (4H, m, CH_2), 2.05 (2H, m, CH_2), 3.53 (1H, dd, $J_{6,6} = 10.1$ Hz, $J_{6,5} = 6.5$ Hz, H_6), 3.62 (1H, dd, $J_{6,6} = 10.1$ Hz, $J_{6,5} = 8.3$ Hz, H_6), 4.18 (1H, d, $J_{5,4} = 2.7$ Hz, H_4), 4.30 (1H, ddd, $J_{6,5} = 8.3$ Hz, $J_{6,5} = 6.5$ Hz, $J_{5,4} = 2.7$ Hz, H_5), 4.66 (1H, m, H_2), 5.50 (1H, d, $J_{8cis,7} = 10.9$ Hz, H_{8cis}), 5.52 (1H, d, $J_{8trans,7} = 17.7$ Hz, H_{8trans}), 5.62 (1H, br s, NH), 5.92 (1H, d, $J_{2,1} = 3.8$ Hz, H_1), 6.07 (1H, dd, $J_{8trans,7} = 17.7$ Hz, $J_{8cis,7} = 10.9$ Hz, H_7), 8.45 (1H, br s, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ −5.5 (2 × C), −5.1, −4.4, 18.1, 18.4, 23.5, 23.6, 25.8 (3 × C), 26.1 (3 × C), 26.3, 26.6, 33.0 (2 × C), 57.1, 63.3, 70.4, 74.3, 78.8, 84.2, 104.1, 112.1, 119.8, 132.0, 180.6. Anal. Calcd for $C_{29}H_{56}N_2O_5SSi_2$: C, 57.95; H, 9.39; N, 4.66; S, 5.33. Found: C, 58.06; H, 9.20; N, 4.49; S, 5.40.

4.4. Computational details

In this work, DFT calculations were carried out using the B3LYP[9,10] exchange-correlation functionals, together with the standard 6-31G(d) basis set. Reactants, the products and transition structures of the [3,3]-sigmatropic rearrangements were optimized at B3LYP/6-31G* level.

The frequencies were computed at B3LYP/6-31G* level. All minima and transition structures were confirmed to have no or one imaginary frequency, respectively. The normal mode corresponding to the imaginary frequency in the case of particular transition structures was found to involve vibrations of the new bond (C–N) being formed. The unscaled zero-point energy corrections (ZPE) from B3LYP/6-31G* level were added to the single point energies calculated at B3LYP/6-311+G** level.

The solvent effect was studied by calculating single point energy of the B3LYP/6-31G* optimized stationary points at B3LYP/6-311+G** level using selfconsistent reaction field (SCRF) method[11,12] based on Tomasi's integral equation formalism polarizable continuum model (pcm).[13] The dielectric constant used in the latter calculations, $\varepsilon = 2.379$, corresponds to toluene. To the energy thus obtained was added the unscaled ZPE calculated at B3LYP/6-31G* level for the gas phase. All calculations were carried out with Gaussian 03 package of programs.[14]

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