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ASYMMETRIC INDUCTION IN [2+2]CYCLOADDITION OF CHLOROSULFONYL ISOCYANATE TO 1,2-*O*-ISOPROPYLIDENE-5-*O*-VINYL-D-GLYCOFURANOSES.

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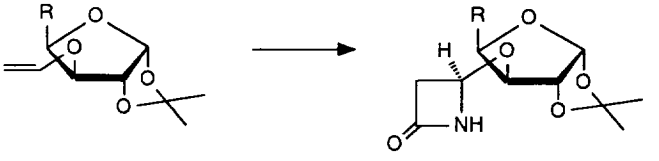
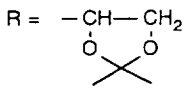
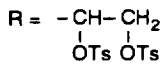
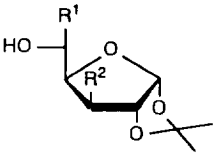
Abstract: The asymmetric [2+2]cycloaddition of chlorosulfonyl isocyanate to 1,2-*O*-isopropylidene-5-*O*-vinyl-D-glycofuranoses is presented. The stereoselectivity strongly depends on substitution and configuration at the C-3 carbon atom. A small substituent at C-3 or allo configuration of the sugar promote excellent stereoselectivity, affording (S) configuration at the C-4' carbon atom of the azetidinone ring. Intramolecular cyclization in compounds **20**, **22-26**, and **31** provides the respective clavams **32-38**.

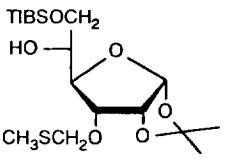
Recently we have reported on the formation of a β-lactam *via* asymmetric [2+2]cycloaddition of chlorosulfonyl isocyanate to 3-*O*-vinyl ethers derived from diacetone D-glucose **1**.[1] Cycloadditions have been performed in the presence of anhydrous sodium carbonate as an agent neutralizing acidic contaminations present in the commercially available reagent.[1,2] The 4'R diastereomer of azetidinones **2** has been obtained predominantly. High stereoselectivity found for **1d** and **1e** has been assigned to the steric effect of the substituent at C-4 of the furanoid ring.



R = 	**1a**	**2a**
$R = CH_2OTs$	**1b**	**2b**
$R = CH_2OTIBS$	**1c**	**2c**
$R = CH_2OSiPh_3$	**1d**	**2d**
R = 	**1e**	**2e**

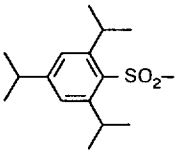
In the present studies we selected as model compounds the 5-*O*-vinyl derivatives of 1,2,-*O*-isopropylidene-α-D-glycofuranoses **10-17**, obtained according to the known procedure[3] from the respective 5-hydroxyprecursors **3-9**.

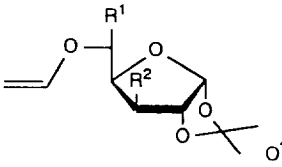


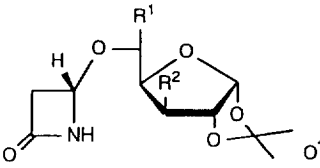


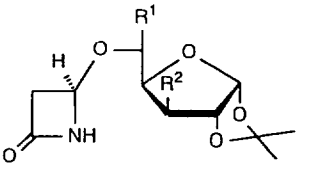
R^1= CH_2OTIBS, R^2= OBzh	**3**
R^1= CH_2OTIBS, R^2= OBn	**4**
R^1= CH_2OTIBS, R^2= OCH_2SCH_3	**5**
R^1= CH_2OTIBS, R^2= OCH_3	**6**
R^1= CH_2OTIBS, R^2= H	**7**
R^1= CH_3, R^2= OBzh	**8**

9

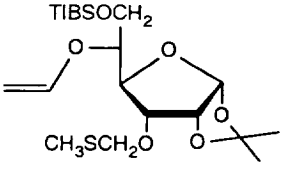
TIBS = 



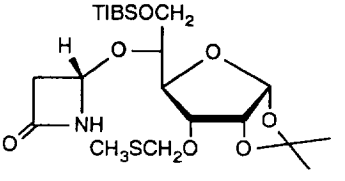




R^1= CH_2OTIBS, R^2= OBzh	**10**	**18**	**19**
R^1= CH_2OTIBS, R^2= OBn	**11**	**20**	**21**
R^1= CH_2OTIBS, R^2= OCH_2SCH_3	**12**	**22**	**23**
R^1= CH_2OTIBS, R^2= OCH_3	**13**	**24**	**25**
R^1= CH_2OTIBS, R^2= H	**14**	**26**	-
R^1= CH_3, R^2= OBzh	**15**	**27**	**28**
R^1= H, R^2= $OSiPh_3$	**16**	**29**	**30**



17



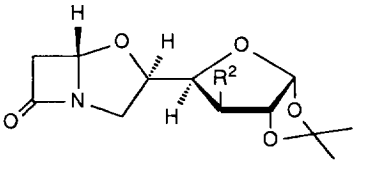
31

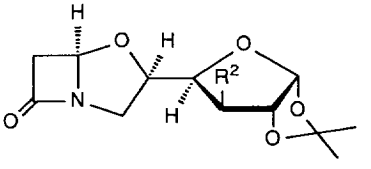
Compounds **3-9** were obtained from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose using standard sequences of reactions (Cf. Experimental). Compound **16** was used as a mixture of two regioisomers (33% of **16** and 67% of **1d**), which was obtained according to Ref. 1. Cycloadditions of chlorosulfonyl isocyanate

to vinyl ethers **10-17** were performed in toluene solution at -78°C in the presence of sodium carbonate. The chlorosulfonyl group was removed from the nitrogen atom of the adduct by Red-Al reduction.

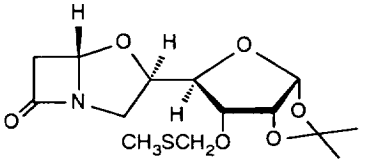
The results of [2+2]cycloaddition of chlorosulfonyl isocyanate to 5-*O*-vinyl furanoses **10-17** are shown in Table 1.

The configurations of compounds **20**, **21**, **22**, **22**, **23**, **24**, **26** and **31** were proved by intramolecular alkylation leading to the respective clavams **32-38**, followed by NOE measurements. Alkylation was carried out in a good yield using a two - phase system (anhydrous potassium carbonate/tetrabutylammonium bromide) in acetonitrile. Configurations of **27**, **28**, **29** and **30** were assigned on the assumption that in the case of **15** and **16** the preferred direction of cycloaddition should be opposite to the tendency demonstrated for vinyl ethers **10-14**.





R^2= OBn	**32**	**33**
R^2= OCH_2SCH_3	**34**	**35**
R^2= OCH_3	**36**	-
R= H	**37**	-



38

The results presented in Table 1 show that stereoselectivity of [2+2]cycloaddition is controlled. A small substituent at the C-3 carbon atom on the top side of the furanose ring or even a large substituent localized on the bottom side give excellent asymmetric induction. This evident relationship between the value and direction of asymmetric induction (Table 1), on the one hand, and configuration of the C-3 on the other, a indicates that the attack of isocyanate occurs from the side occupied by the R^2 substituent. The S configuration of the main diastereomer formed proves that the *re* side of the olefin is turned in the R^2 substituent and the *si* side is blocked by the TIBS group. The character of this blocking could be assigned to complexation of the nucleophilic olefin by the electrophilic aryl substituent (Fig. 1).

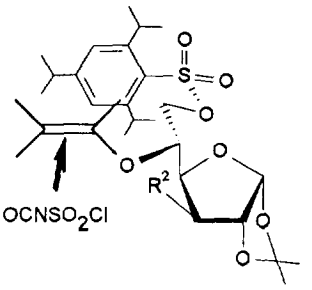


Fig 1.

Size diminution of the R^2 substituent (Fig. 1) opens an access of the isocyanate to the *re* side of the double bond and consequently causes predominance of the 4'S diastereomers **20**, **22**, and **24**. In the case of the 3-deoxy compound **14** or allo configuration of the substrate **17** only one diastereomer is formed, **26** or **31**, respectively.

Diminution of size of the terminal substituent by transformation of arylsulfonyloxymethyl into a methyl group (**15**) etiminates complexation of the olefin and should open an entry to the *si* side of the double bond. Consequently, we assume that the prevailing diastereomer **28** has a R configuration at the C-4' carbon atom of the azetidinone ring. It should, however, be stressed that the absence of the arylsulfonyl group may cause significant changes in the conformation of the transition state, and in this case the proposed explanation and assumed configuration of azetidinone moiety would not be justified. Removal of the C-6 carbon atom and introduction of the large 3-*O*-triphenylsilyl substituent (**16**) lead to a further decrease in the face-differentiation of the double bond. The interaction between the electrophilic arene and nucleophilic olefin seems to be the crucial factor that controls the stereoselectivity of [2+2]cycloaddition. So far, however, there is no direct evidence for such a charge - transfer interaction. The interaction between the electrophilic olefin and the phenyl ring has been postulated to be the sole factor responsible for the high selectivity of the addition of organocuprates to α,β-unsaturated esters derived from 5-deoxy-5-phenyl-1,2-*O*-isopropylidene-α-D-ribopentofuranose.[4]

The present results show that 5-*O*-vinyl ethers of 1,2-isopropylidene-α-D-glycofuranose can offer excellent asymmetric induction in [2+2]cycloaddition with chlorosulfonyl isocyanate, and that the direction of induction is complementary to that found for 3-*O*-vinyl congeners[1] (4'S versus 4'R).

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

Substrate	T (°C)	Time (min)	Products	Yield (%)	Diastereoselectivity (% of resp. adducts)
10	-78	100	**18** : **19**	52	54 : 46
	-40	60	**18** : **19**	60	50 : 50
11	-78	90	**20** : **21**	51	86 : 14
	-40	30	**20** : **21**	49	82 : 18
12	-78	60	**22** : **23**	52	69 : 31
13	-78	60	**24** : **25**	50	96 : 4
14	-78	75	**26**	43	97 <
15	-78	60	**27** : **28**	51	30 : 70
16	-78	60	**29** : **30**	50	36 : 64
17	-78	60	**31**	53	97 <

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).

Synthesis of 5-*O*-unsubstituted compounds 3-9. Compounds **3-7** were obtained from the respective 3-substituted-1,2-*O*-isopropylidene-α-D-glycofuranoses (12 mmol) by treatment with 2,4,6-triisopropylbenzenesulfonyl chloride (16 mmol) in pyridine solution (20 ml) at 0°C, overnight. The standard work up followed by chromatographical purification afforded compounds **3-7** in about 70% yield.

6-*O*-(Triisopropylbenzenesulfonyl)-1,2-*O*-isopropylidene-3-*O*-diphenylmethyl-α-D-glucofuranose (3): syrup; $[\alpha]_D$ -25.8 (*c* 2.2, CH_2Cl_2); IR ($CHCl_3$): 3580 cm^{-1}; ^{1}H NMR ($CDCl_3$): 4.02 (dd, 1H, *J* 3.2, 8.4 Hz, H-4), 4.8 (dd, 1H, *J* 7.4, 10.5 Hz, H-6a), 4.15 (d, 1H, *J* 3.2 Hz, H-3), 4.31 (m, 1H, H-5), 4.34 (dd, 1H, *J* 2.5, 10.5 Hz, H-6b), 4.52 (d, 1H, *J* 3.7 Hz), 5.57 (s, 1H, $CHPh_2$), 5.89 (d, 1H, *J* 3.7 Hz, H-1); MS (EI, HR) m/z: M-17, found: 635.30422. Calcd for $C_{37}H_{47}O_7S$: 635.30424.

3-*O*-Benzyl-6-*O*-(triisopropylbenzenesulfonyl)-1,2-*O*-isopropylidene-α-D-glucofuranose (**4**): syrup; $[\alpha]_D$ -16.4 (*c* 2.1, CH_2Cl_2); IR (film): 3582 cm^{-1}; ^1H NMR ($CDCl_3$): 4.08 (dd, 1H, *J* 3.3, 7.9 Hz, H-4), 4.09-4.17 (m, 4H, H-6a, 2 C<u>H</u>$(CH_3)_2$), 4.25 (m, 1H, H-5), 4.31 (dd, 1H, *J* 2.9, 10.5 Hz, H-6b), 4.58 (d, 1H, *J* 3.7 Hz, H-2), 4.58, 4.70 (2d, 2H, *J* 11.6 Hz, Benzyl), 5.88 (d, 1H, *J* 3.7 Hz, H-1); MS (EI, HR) m/z: M-15, found: 561.2520. Calcd for $C_{30}H_{41}O_8S$: 561.25221.

6-*O*-(Triisopropylbenzenesulfonyl)-1,2-*O*-isopropylidene-3-*O*-methylthiometyl-α-D-glucofuranose (**5**): syrup; $[\alpha]_D$ -41.8 (*c* 1.4, CH_2Cl_2); IR ($CHCl_3$): 3405 cm^{-1}; ^1H NMR ($CDCl_3$): 2.20 (s, 3H, SCH_3), 4.03-4.24 (m, 5H, H-6a, H-4, H-5, $2CHMe_2$), 4.27-4.40 (m, 2H, H-3, H-6b), 4.56 (d, 1H, *J* 3.8 Hz, H-2), 4.67, 4.81 (2d, 2H, *J* 11.8 Hz, CH_2S), 5.86 (d, 1H, *J* 3.6 Hz, H-1); MS (EI, HR) m/z: M-15, found: 531.20857. Calcd for $C_{25}H_{39}O_8S_2$: 531.20863.

6-*O*-(Triisopropylbenzenesulfonyl)-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-glucofuranose (**6**): syrup; $[\alpha]_D$ -50.4 (*c* 1.3, CH_2Cl_2); IR (film): 3526 cm^{-1}; ^1H NMR ($CDCl_3$): 3.45 (s, 3H, OCH_3), 3.92 (d, 1H, *J* 3.2 Hz, H-3), 4.04-4.34 (m, 6H, H-4,5,6a,6b, $2CHMe_2$), 4.57 (d, 1H, *J* 3.8 Hz, H-2), 5.87 (d, 1H, *J* 3.8 Hz, H-1); MS (EI, HR) m/z: M-15, found 485.2209. Calcd for $C_{24}H_{37}O_8S$: 485.22091.

3-Deoxy-6-*O*-(triisopropylbenzenesulfonyl)-1,2-*O*-isopropylidene-α-D-ribohexofuranose (**7**): syrup; $[\alpha]_D$ -5.8 (*c* 1.3, CH_2Cl_2); IR (film): 3426 cm^{-1}; ^1H NMR ($CDCl_3$): 1.83 (ddd, 1H, *J* 4.7, 10.4, 13.5 Hz, H-3a), 2.15 (dd, 1H, 4.6, 13.5 Hz, H-3b), 3.96-4.25 (m, 6H, H-4.5, 6a, 6b, $CHMe_2$), 4.74 (t, 1H, *J* 3.6, 4.7 Hz, H-2), 5.78 (d, 1H, *J* 3.6 Hz, H-1); MS (EI, HR) m/z: M-15, found: 455.2103. Calcd for $C_{23}H_{35}O_7S$: 455.2103.

6-*O*-(Triisopropylbenzenesulfonyl)-1,2-*O*-isopropylidene-3-*O*-methylthiomethyl-α-D-allofuranose (**9**): was obtained according to the same procedure from 3-*O*-methylthiomethyl α-D-allofuranose syrup;$[\alpha]_D$ 75.0 (*c* 0.6, CH_2Cl_2); IR ($CHCl_3$): 3580 cm^{-1}; ^1H NMR ($CDCl_3$): 2.10 (s, 3H, SCH_3), 4.08-4.28 (m, 7H, H-3,4,5,6a,6b, $2CHMe_2$), 4.66, 4.76 (2d, 2H, *J* 11.9 Hz, CH_2S), 4.69 (t, 1H, *J* 3.3, 4.6 Hz, H-2), 5.76 (d, 1H, *J* 4.6 Hz, H-1); MS (EI, HR) m/z: M-15, found: 531.20858. Calcd for $C_{25}H_{39}O_8S_2$: 531.20863.

6-Deoxy-1,2-isopropylidene-3-*O*-diphenylmethyl-α-D-glucofuranose (**8**). To a solution of $LiAlH_4$ (0.05 g, 1.10 mmol) in dry tetrahydrofurane (20 ml) under dry argon compound **10** (1.02 g, 1.57 mmol) in dry tetrahydrofurane (10 ml) was added dropwise. The mixture was refluxed for 20 min. Subsequently it was cooled to room temperature and treated successively with water (1 ml), 15% sodium hydroxide (1 ml), and water (1 ml). Filtration through Cellite, followed by concentration and chromographical purification prowided **8** (0.45 g, 78%): syrup; $[\alpha]_D$ -77.1 (*c* 0.4, CH_2Cl_2); IR (film): 3500 cm^{-1} ;^1H NMR ($CDCl_3$): 1.22 (d, 3H, CH_3), 3.89 (dd, 1H, *J* 3.2, 7.6 Hz, H-4), 4.13 (d, 1H, *J* 3.2 Hz, H-3), 4.15 (m, 1H, H-5), 4.12 (d, 1H, *J* 3.9

Hz, H-2), 5.99 (d, 1H, *J* 3.9 Hz, H-1); MS (EI, HR) m/z: $M^{+\cdot}$; found 370.17819. Calcd for $C_{22}H_{26}O_5$: 370.17802.

5-*O*-Vinyl ethers **10-16** were obtained from proper 5-hydroxy precursors **3-9** using a known mercury acetate catalyzed transetherification method.[3]

6-*O*-(Triisopropylbenzenesulfonyl)-1,2-*O*-isopropylidene-3-*O*-diphenylmethyl-5-*O*-vinyl-α-D-glucofuranose (10): 25%; $[\alpha]_D$ -17.4 (*c* 1.0, CH_2Cl_2); IR (film): 1638 cm^{-1}; ^1H NMR ($CDCl_3$) inter dia: 3.91 (dd, 1H, *J* 1.9, 6.5 Hz, H-2a'), 4.47 (d, 1H, *J* 3.6 Hz, H-2), 4.57 (dd, 1H, *J* 2.0, 10.7 Hz, H-6b), 5.48 (s, 1H, $CHPh_2$), 5.84 (d, 1H, *J* 3.6 Hz, H-1), 6.08 (dd, 1H, *J* 6.5, 14.0 Hz, H-1'); MS (EI, HR) m/z: M-15, found: 663.29908. Calcd for $C_{38}H_{47}O_8S$: 663.29916.

3-*O*-Benzyl-6-*O*-(triisopropylbenzenesulfonyl)-1,2-*O*-isopropylidene-5-*O*-vinyl-α-D-glucofuranose (11): 69%; $[\alpha]_D$ -17.8 (*c* 1.7, CH_2Cl_2); IR ($CHCl_3$): 1638 cm^{-1}; ^1H NMR ($CDCl_3$): 3.99 (dd, 1H, *J* 1.9, 6.4 Hz, H-2a'), 4.01 (d, 1H, *J* 3.2 Hz, H-3), ~4.15 (m, 1H, H-6a), 4.17 (dd, 1H, *J* 3.2, 3.7 Hz, H-4), 4.29 (dd, 1H, *J* 1.9, 13.9 Hz, H-2b'), 4.38 (ddd, 1H, *J* 2.1, 6.9, 8.7 Hz, H-5), 4.48 (dd, 1H, *J* 2.1, 11.0 Hz, H-6b), 4.52, 4.60 (2d, 2H, *J* 11.4 Hz, Benzyl), 4.56 (d, 1H, *J* 3.7 Hz, H-2), 5.85 (d, 1H, *J* 3.7 Hz, H-1), 6.22 (dd, 1H, *J* 6.4, 13.9 Hz, H-1'); MS (EI, HR) m/z: M-15, found: 587.26788. Calcd for $C_{32}H_{43}O_8S$: 587.26786.

6-*O*-(Triisopropylbenzenesulfonyl)-1,2-*O*-isopropylidene-3-*O*-methylthiomethyl-5-*O*-vinyl-α-D-glucofuranose (12): 72%; $[\alpha]_D$ -9.8 (*c* 1.3, CH_2Cl_2); IR (CCl_4) 1637 cm^{-1}; ^1H NMR ($CDCl_3$) *inter alia*: 4.04 (dd, 1H, *J* 1.9, 6.5 Hz, H-2'a), 4.50 (dd, 1H, *J* 1.9, 10.9 Hz, H-6b), 4.62 (d, 1H, *J* 3.7 Hz, H-2), 4.65, 4.70 (2d, 2H, *J* 11.8 Hz, CH_2SMe), 5.84 (d, 1H, *J* 3.7 Hz, H-1), 6.28 (dd, 1H, *J* 6.5, 13.9 Hz, H-1'); MS (LSIMS, HR) m/z: M+Na, found: 595.236722. Calcd for $C_{28}H_{44}O_8S_2Na$: 595.236722.

6-*O*-(Triisopropylbenzenesulfonyl)-1,2-*O*-isopropylidene-3-*O*-methyl-5-*O*-vinyl-α-D-glucofuranose(13); 85%; $[\alpha]_D$ -20.9 (*c* 1.9, CH_2Cl_2); IR ($CHCl_3$): 1637 cm^{-1}; ^1H NMR ($CDCl_3$): 3.36 (s, 3H, OCH_3), 3.73 (d, 1H, *J* 3.2 Hz, H-3), 4.00 (dd, 1H, *J* 1.8, 6.4 Hz, H-2'a), 4.05-4.23 (m, 4H, H-4,6a, $2CHMe_2$), 4.32 (dd, 1H, *J* 1.8, 13.9 Hz, H-2'b), 4.33 (m, 1H, H-5), 4.44 (dd, 1H, *J* 1.9, 10.7 Hz, H-6b), 4.54 (d, 1H, *J* 3.8 Hz, H-2), 5.83 (d, 1H, *J* 3.8 Hz, H-1), 6.25 (dd, 1H, *J* 6.4, 13.9 Hz, H-1'); MS (EI, HR) m/z: $M^{+\cdot}$, found: 527.26760. Calcd for $C_{27}H_{43}O_8S$: 527.26706.

3-Deoxy-6-*O*-(triisopropylbenzenesulfonyl)-1,2-*O*-isopropylidene-5-*O*-vinyl-α-D-ribohexofuranose (14): 70%; $[\alpha]_D$ -3.6 (*c* 1.0, CH_2Cl_2); IR (film) 1638 cm^{-1}; ^1H NMR ($CDCl_3$): 1.82 (ddd, 1H, *J* 4.7, 10.4, 13.4 Hz, H-3a), 2.14 (dd, 1H, *J* 4.7, 13.4 Hz, H-3b), 4.00 (dd, 1H, *J* 1.9, 6.4 Hz, H-2'a), 4.00-4.34 (m, 6H, H-

4,5,6a,6b, $2CHMe_2$), 4.30 (dd, 1H, *J* 1.9, 13.9 Hz, H-2'b), 4.72 (t, 1H, *J* 3.6, 4.7 Hz, H-2), 5.75 (d, 1H, *J* 3.6 Hz, H-1), 6.27 (dd, 1H, *J* 6.4, 13.9 Hz, H-1'): MS (EI, HR) m/z: M-15, found 481.22560. Calcd for $C_{25}H_{37}O_7S$: 481.22599.

6-Deoxy-1,2-*O*-isopropylidene-3-O-diphenylmethyl-5-*O*-vinyl-α-D-glucofuranose (15); $[\alpha]_D$ -28.9 (*c* 0.6, CH_2Cl_2); IR ($CHCl_3$): 1636 cm^{-1}; ^1H NMR ($CDCl_3$): 1.38 (d, 3H, *J* 6.2 Hz, CH_3), 4.00 (dd, 1H, *J* 1.7, 6.6 Hz, H-2'a), 4.04 (dd, 1H, *J* 3.0, 8.6 Hz, H-4), 4.08 (d, 1H, *J* 3.0 Hz, H-3), 4.27 (dd, 1H, *J* 1.7, 14.1 Hz, H-2'b), 4.35 (dq, 1H, *J* 6.2, 8.6 Hz, H-5), 4.54 (d, 1H, *J* 3.7 Hz, H-2), 5.91 (d, 1H, *J* 3.7 Hz, H-1), 6.17 (dd, 1H, *J* 6.6, 14.1 Hz, H-1'); MS (EI, HR) m/z: $M^{+\cdot}$, found 396.19373. Calcd for $C_{24}H_{28}O_5$: 396.19367; M-15, found: 381.1703. Calcd for $C_{23}H_{25}O_5$: 381.1702.

6-*O*-(Triisopropylbenzenesulfonyl)-1,2-*O*-isopropylidene-3-*O*-methylthiomethyl-5-*O*-vinyl-α-D-allofuranose (17); 78%; $[\alpha]_D$ 69.7 (*c* 0.3, CH_2Cl_2); IR ($CHCl_3$): 1638 cm^{-1}; ^1H NMR ($CDCl_3$): 4.00 (dd, 1H, *J* 1.9, 6.4 Hz, H-2a'), 4.02-4.40 (m, 7H, H-3,4,5,6a,6b, $2CHMe_2$), 4.35 (dd, 1H, *J* 1.9, 13.9 Hz, H-2'b), 4.67 (t, 1H, *J* 3.2, 3.6 Hz, H-2), 4.66, 4.73 (2d, 2H, *J* 11.8 Hz, CH_2SMe), 5.73 (d, 1H, *J* 3.6 Hz, H-1), 6.27 (dd, 1H, *J* 6.4, 13.9 Hz, H-1'); MS (EI, HR) m/z: M-15, found: 557.2240. Calcd for $C_{27}H_{41}O_8S_2$: 557.22428.

Compound **16** was obtained according to the procedure described earlier[1] and used for cycloaddition as a mixture containing 30% of **16** and 70% of **1d**.

[2+2]Cycloaddition of chlorosulfonyl isocyanate to vinyl ethers 10-17. General procedure. To a suspension of anhydrous sodium carbonate (0.08 g) in anhydrous toluene (1 ml) chlorosulfonyl isocyanate (61 μl, 0.7 mmol) was added. Upon stirring, and cooling to -78°C a solution of vinyl ether **10-17** (0.5 mmol) in toluene (1 ml) was added dropwise. Subsequently the temperature of the mixture was allowed to rise to -40°C and it was maintained for 1 h. With stirring, the suspension was cooled to -78°C, diluted with toluene (5 ml), treated with Red-Al (1 ml of a 1M solution in toluene), and left for 30 min whereas the temperature of reaction (-78°C) was maintained. Subsequently the temperature was allowed to rise to 0°C, water (0.4 ml) was added, and the mixture was stirred for 45 min. The organic layer was separated, washed, dried, and evaporated. The crude residue was purified on silica gel.

(**4'S**) and (**4'R**) **5-*O*-(Azetidin-2'onyl-4')-6-*O*-triisopropylbenzenesulfonyl-1,2-*O*-isopropylidene-3-*O*-diphenylmethyl-α-D-glucofuranose** (**18** and **19**): IR (CCl_4): 1789 cm^{-1}; ^1H NMR ($CDCl_3$) taken as a mixture, *inter alia*, major ~54%: 2.48 (bd, 1H, *J* 14.9 Hz, H-3'a), 2.53 (dd, 1H, *J* 2.5, 3.9, 14.9 Hz, H-3'b), 4.76 (dd, *J* 1.5, 3.9 Hz, H-4'), 5.43 (s, 1H, $CHPh_2$), 5.80 (d, 1H, *J* 3.7 Hz, H-1); minor isomer 46%, 2.76 (dd, 1H, *J* 1.2 Hz, H-3'a), 3.00 (dt, 1H, *J* 3.1, 3.8, 15.2 Hz, H-3'b), 4.99 (dd, 1H, *J* 1.2, 3.8 Hz, H-4'), 5.47

(s, 1H, $CHPh_2$), 5.78 (d, 1H, *J* 3.6 Hz, H-1); MS (EI, HR) m/z: $M^{+\cdot}$, found: 721.32809. Calcd for $C_{40}H_{51}NO_9S$: 721.328455.

(**4'S**) and (**4'R**) **5-*O*-(Azetidin-2'-onyl-4')-3-*O*-benzyl-6-*O*-triisopropylbenzenesulfonyl-1,2-*O*-isopropylidene-α-D-glucofuranose** (**20** and **21**); IR ($CHCl_3$): 1773 cm^{-1}; ^1H NMR ($CDCl_3$) taken as a mixture, *inter alia*: major ~86%, 2.82 (dd, 1H, *J* 1.1, 15.2 Hz, H-3'a), 3.07 (dd, 1H, *J* 2.9, 3.9, 15.2 Hz, H-3'b), 4.41 (dd, 1H, *J* 1.8, 11.0 Hz, H-4), 4.44, 4.77 (2d, 1H, *J* 11.8 Hz, Benzyl), 4.65 (d, 1H, *J* 3.8 Hz, H-2), 5.19 (dd, 1H, *J* 1.2, 3.9 Hz, H-4'), 5.68 (bs, 1H, NH), 5.86 (d, 1H, *J* 3.8 Hz, H-1): minor isomer ~14%; 2.68 (dd, 1H, *J*1.4, 15.2 Hz, H-3a), 2.84 (ddd, 1H, *J* 2.6, 4.0, 15.2 Hz, H-3'b), 4.62 (d, 1H, *J* 3.7 Hz, H-2), 5.04 (dd, 1H, *J* 1.4, 4.0 Hz, H-4'), 5.85 (d, 1H, *J* 3.7 Hz, H-1). MS (EI,HR) m/z taken as a mixture, $M^{+\cdot}$: 645.29723. Calcd for $C_{34}H_{47}NO_4S$: 645.297154.

(**4'S**) and (**4'R**) **5-*O*-(Azetidin-2'-onyl-4')-6-*O*-triisopropylbenzenesulfonyl-1,2-*O*-isopropylidene-3-*O*-methylthiometyl-α-D-glucofuranose** (**22** and **23**); IR ($CHCl_3$): 1773 cm^{-1}; ^1H NMR ($CDCl_3$) taken as a mixture, *inter alia*: major isomer ~69%, 2.24 (s, 3H, SCH_3), 3.17 (ddd, 1H, *J* 2.7, 3.9, 15.2 Hz, H-3'b), 4.61 (d, 1H, *J* 3.7 Hz, H-2), 5.36 (dd, *J* 1.4, 3.9 Hz, H-4'), 5.82 (d, 1H, *J* 3.7 Hz, H-1); minor isomer ~31%, 2.21 (S, 3H, SCH_2), 3.14 (ddd, 1H, *J* 2.6, 4.0, 14.9 Hz, H-3'b), 5.23 (dd, 1H, *J* 1.5, 4.0 Hz, H-4').
MS (EI, HR) m/z: M-15, found 600.23003. Calcd for $C_{28}H_{42}NO_9S_2$: 600.23016.

(**4'S**) and (**4'R**) **5-*O*-(Azetidin-2'-onyl-4')-6-*O*-triisopropylbenzenesulfonyl-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-glucofuranose** (**24** and **25**); IR (CCl_4): 1788 cm^{-1}; ^1H NMR ($CDCl_3$) taken as a mixture, major isomer 96%, 2.83-3.00 (m, 2H, H-3'a, $CHMe_2$), 3.17 (ddd, 1H, *J* 2.7, 3.8, 15.2 Hz, H-3'b), 3.42 (s, 3H, OCH_3), 3.79 (d, 1H, *J* 3.0, H-3), 3.96-4.46 (m, 6H, H-4,5,6a, 6b, $2CHMe_2$), 4.57 (d, 1H, *J* 3.8 Hz, H-2), 5.43 (dd, 1H, *J* 1.4, 3.8 Hz, H-4'), 5.81 (d, 1H, *J* 3.8 Hz, H-1); minor isomer 4%, *inter alia*: 5.22 (dd, 1H, *J* 1.5, 3.9 Hz, H-4'): MS (EI, HR), m/z: $M^{+\cdot}$, found: 554.2422. Calcd for $C_{27}H_{40}NO_9S$: 554.24238.

(**4'S**) **5-*O*-(Azetidin-2'-onyl-4')-3-deoxy-6-*O*-triisopropylbenzenesulfonyl-1,2-*O*-isopropylidene-α-D-ribohexofuranose** (**26**); $[\alpha]_D$ -4.7 (*c* 1.1, CH_2Cl_2); IR ($CHCl_3$): 1773 cm^{-1}; ^1H NMR ($CDCl_3$): 1.85 (ddd, 1H, *J* 4.7, 10.7, 13.2 Hz, H-3a), 1.00 (dd, 1H, *J* 4.5, 13.2 Hz, H-3b), 2.84 (ddd, 1H, *J* 0.6, 1.4, 15.2 Hz, H-3'a), 3.10 (ddd, 1H, *J* 2.6, 4.0, 15.2 Hz, H-3'b), 3.97 (dd, 1H, *J* 7.5, 10.7 Hz, H-6a), 4.03-4.15 (m, 4H, H-5, 6b, $2CHMe_2$), 4.19 (dt, 1H, H-4), 4.74 (t, 1H, H-2), 5.19 (dd, 1H, *J* 1.4, 4.0 Hz, H-4'), 5.75 (d, 1H, *J* 3.6 Hz, H-1). MS (EI,HR), m/z: $M^{+\cdot}$, found: 539.2553. Calcd for $C_{27}H_{41}NO_8S$: 539.25528.

(**4'S**) and (**4'R**) **5-*O*-(Azetidin-2'-onyl-4')-6-deoxy-1,2-*O*-isopropylidene-3-*O*-diphenylmethyl-α-D-glucofuranose** (**27** and **28**). IR ($CHCl_3$): 1771 cm^{-1}; ^1H NMR ($CDCl_3$) taken as a mixture, *inter alia*: minor

isomer **27**, 30%: 1.31 (d, 3H, *J* 6.1 Hz, CH_3), 2.72 (ddd, 1H, 0.6, 1.4, 14.9 Hz, H-3'a), 2.99 (ddd, 1H, *J* 2.8, 3.8, 14.9 Hz, H-3'b), 4.16 (d, 1H, *J* 2.8 Hz, H-3), 4.40 (d, 1H,*J* 3.7 Hz, H-2), 4.84 (dd, 1H, *J* 1.4, 3.8 Hz, H-4), 5.49 (s, 1H, $CHPh_2$), 5.87 (d, 1H, *J* 3.7 Hz, H-1); major isomer **28**, 70%: 1.34 (d, 3H, *J* 6.1 Hz, CH_3), 2.56 (ddd, 1H, *J* 0.4, 1.6, 15.0 Hz, H-3'a), 2.69 (ddd, 1H, *J* 3.0, 4.1, 15.0 Hz, H-3'b), 4.13 (d, 1H, *J* 3.0 Hz, H-3), 4.47 (d, 1H, *J* 3.7 Hz, H-2), 4.79 (dd, 1H, *J* 1.6, 4.1 Hz, H-4'), 5.88 (d, 1H, *J* 3.7 Hz, H-1): MS (EI, HR) m/z: M-15, found: 427.1760. Calcd for $C_{24}H_{26}NO_6$: 424.17601.

(**4'S**) and (**4'R**) **5-*O*-(Azetidin-2'-onyl-4')-1,2-*O*-isopropylidene-3-*O*-triphenylsilyl-α-D-xylopentofuranose** (**29** and **30**). IR ($CHCl_3$): 1775 cm^{-1}; ^1H NMR ($CDCl_3$) taken as a mixture of **2d**, **29** and **30**, *inter alia*: minor isomer **29**, 36%: 4.91 (dd, 1H, *J* 4.0, 1.5 Hz, H-4'), 5.94 (d, 1H, *J* 3.6 Hz, H-1); major isomer **30**, 64%: 4.94 (dd, 1H, *J* 3.9, 1.5 Hz, H-4'), 5.97 (d, 1H, *J* 3.5 Hz, H-1).

(**4'S**) **5-*O*-(Azetidin-2'-onyl-4')-6-*O*-triisopropyl-benzenesulfonyl-1,2-*O*-isopropylidene-3-*O*-methylthiomethyl-α-D-allofuranose** (**31**). $[\alpha]_D$ 61.8 (*c* 0.3, CH_2Cl_2); IR ($CHCl_3$): 1773 cm^{-1}; ^1H NMR ($CDCl_3$): 2.02 (s, 3H, SCH_3), 2.90 (bd, 1H, H-3'a), 3.11 (ddd, 1H, *J* 2.5, 4.0, 15.2 Hz, H-3'b), 4.03 (dd, 1H, *J* 1.8, 8.9 Hz, H-6a), 4.05-4.11 (m, 4H, H-3,5, $2CHMe_2$), 4.17 (bd, 1H, H-6b), 4.21 (dd, 1H, *J* 4.2, 9.0 Hz, H-4), 4.63, 4.68 (2d, 2H, *J* 11.8 Hz, CH_2S), 4.70 (t, 1H, H-2), 5.15 (dd, 1H, H-2), 5.15 (dd, 1H, *J* 1.4, 4.0 Hz, H-4'), 5.73 (d, 1H, *J* 3.6 Hz, H-1); MS (EI, HR) m/z: M-15, found: 600.23003. Calcd for $C_{28}H_{42}NO_9S_2$: 600.23009.

Cyclization of compounds 20-26 and **31**; **general procedure**. Compounds **20-26**, and **31** (0.31 mmol) were dissolved in acetonitrile (15 ml) and treated with tetrabutylammonium bromide (0.15 g) and pulverized anhydrous K_2CO_3 (1.5 g). The mixture was stirred and kept under reflux for 15 min. Subsequently it was cooled, filtered, concentrated, and treated with toluene (15 ml). The solution was washed with water, dried, and evaporated. The crude product was separated on silica gel to afford the respective products **32-38** in about 85% yield.

(**2'R, 5'S**) and (**2'R, 5'R**) **3-*O*-Benzyl-4-*C*-(clavamyl-2')-1,2-isopropylidene-α-D-xylotetrofuranose** (**32** and **33**) were obtained from a mixture of **20** and **21** according to the above procedure chromatographical separation afforded **32** (80%) and **33** (20%).

32: $[\alpha]_D$ -110.7 (*c* 1.1, CH_2Cl_2); IR ($CHCl_3$): 1778 cm^{-1}; ^1H NMR ($CDCl_3$): 1.32, 1.49 (2s, 6H, isopr.), 2.80 (dd, 1H, *J* 0.7, 16.1 Hz, H-6'a), 3.12 (ddd, 1H, *J* 0.9, 6.3, 11.9 Hz, H-6a), 3.26 (ddd, 1H, *J* 0.9, 2.7, 16.1 Hz, H-6'b), 3.97 (ddd, 1H, *J* 6.8, 11.9 Hz, H-6b), 4.00 (d, 1H, *J* 3.4 Hz, H-3), 4.30 (dd, 1H, *J* 3.4, 5.5 Hz, H-4), 4.54 (m, 1H, H-5), 4.54, 4.67 (2d, 2H, *J* 11.8 Hz, benzyl), 4.59 (d, 1H, *J* 3.7 Hz, H-2), 5.32 (d, 1H, *J* 2.5 Hz, H-5'), 5.92 (d, 1H, *J* 3.7 Hz, H-1); MS (EI, HR) m/z: $M^{+\cdot}$, found: 361.15268. Calcd for

$C_{19}H_{23}NO_6$: 361.15253.

(2'R, 5'S) and **(2'R, 5'R) 4-*C*-(Clavamyl-2')-1,2-isopropylidene-3-*O*-methylthiomethyl-α-D-xylotetrofuranose (34** and **35)** were obtained from a mixture of **22** and **23** according to the above procedure. Chromatographical seperation afforded **34** (69%); $[\alpha]_D$ -122.3 (*c* 0.3, CH_2Cl_2): IR (CCl_4): 1793 cm^{-1}; ^1H NMR ($CDcl_3$): 1.32, 1.50 (2s, 6H, isopr.), 2.17 (s, 3H, SCH_3), 2.79 (dd, 1H, *J* 0.7, 16.1 Hz, H-6'a), 3.08 (ddd, *J* 0.8, 6.4, 11.9 Hz, H-6a), 3.27 (ddd, 1H, *J* 0.8, 2.7, 16.1 Hz, H-6'b), 3.98 (dd, 1H, *J* 6.7, 11.9 Hz, H-6b), 4.28 (dd, 1H, *J* 3.3, 6.2 Hz, H-4), 4.33 (d, H, *J* 3.3 Hz, H-3), 4.49 (q, 1H, H-5), 4.56 (d, 1H, *J* 3.7 Hz, H-2), 4.64, 4.76 (2d, 2H, *J* 11.7 Hz, benzyl), 5.33 (d, 1H, *J* 2.7 Hz, H-5), 5.90 (d, 1H, *J* 3.7 Hz, H-1); MS (EI, HR) m/z: M-15, found: 316.0856. Calcd for $C_{13}H_{18}NO_6S$: 316.08548.
35 (31%); $[\alpha]_D$ 23.2 (*c* 0.3, CH_2Cl_2), IR(CCl_4): 1794 cm^{-1}; ^1H NMR ($CDCl_3$): 1.32, 1.49 (2s, 6H, isopr.), 2.89 (d, 1H, *J* 16.0 Hz, H-6'a), 3.14 (ddd, 1H, *J* 0.8, 7.0, 11.5 Hz, H-6a), 3.24 (ddd, 1H, *J* 0.8, 2.6, 6.6 Hz, H-6'b), 3.93 (dd, 1H, *J* 5.3, 11.5 Hz, H-6b), 4.16 (dd, 1H, *J* 3.3, 6.9 Hz, H-4), 4.28 (d, 1H, *J* 3.3 Hz, H-3), 4.50 (m, 1H, H-5), 4.56 (d, 1H, *J* 3.7 Hz, H-2), 4.66, 4.76 (2d, 2H, *J* 11.7 Hz, benzyl), 5.19 (d, 1H, *J* 2.3 Hz, H-5'), 5.89 (d, 1H, *J* 3.7 Hz, H-1); MS (EI, HR) m/z: M-15, found: 316.0855. Calcd for $C_{13}H_{18}NO_6S$: 316.08548.

(2'R, 5'S) 4-*C*-(Clavamyl-2')-1,2-isopropylidene-3-*O*-methyl-α-D-xylotetrofuranose (36) was obtained from **24** according to the above procedure; $[\alpha]_D$ -136.4 (*c* 1.2, CH_2Cl_2); IR (CCl_4) 1789 cm^{-1}; ^1H NMR ($CDCl_3$): 1.32, 1.50 (2s, 6H, isopr.), 2.82 (dd, 1H, *J* 0.7, 16.1 Hz, H-6'a), 3.07 (ddd, 1H, *J* 0.9, 6.5, 12.0 Hz, h-6a), 3.26 (ddd, 1H, *J* 0.9, 2.7, 16.1 Hz, H-6'b), 3.41 (s, 3H, SCH_3), 3.77 (d, 1H, *J* 3.4 Hz, H-3), 3.96 (dd, 1H, *J* 6.8, 12.0 Hz, H-6b), 4.27 (dd, 1H, *J* 3.4, 5.8 Hz, H-4), 4.52 (q, 1H, H-5), 4.56 (d, 1H, *J* 3.7 Hz, H-2), 5.33 (d, 1H, *J* 2.7 Hz, H-5'), 5.88 (d, 1H, *J* 3.7 Hz, H-1); MS (EI, HR) m/z: $M^{+\cdot}$; found: 285.12162. Calcd for $C_{13}H_{19}NO_6$: 285.12123.

(2'R, 5'S) 4-*C*-(Clavamyl-2')-3-deoxy-1,2-isopropylidene-α-D-erythrotetrofuranose (37) was obtained from **26** according to the procedure; $[\alpha]_D$ -134.3 (*c* 0.7, CH_2Cl_2); IR ($CHCl_3$): 1780 cm^{-1}; ^1H NMR ($CDCl_3$): 1.32, 1.51 (2s, 6H, isopr.), 1.62 (ddd, 1H, *J* 4.8, 10.6, 13.4 Hz, H-3a), 2.19 (dd, 1H, *J* 4.4, 13.4 Hz, H-3b), 2.84 (dd, 1H, *J* 0.5, 16.2 Hz, H-6'a), 2.89 (ddd, *J* 0.8, 6.3, 11.6 Hz, H-6a), 3.27 (ddd, 1H, *J* 0.9, 2.8, 16.2 Hz, H-6'b), 3.98 (dd, 1H, *J* 6.6, 11.6 Hz, H-6b), 4.24-4.33 (m, 2H, H-2', 4), 4.75 (t, 1H, H-2), 5.34 (d, 1H, *J* 2.8 Hz, H-5'), 5.82 (d, 1H, *J* 3.6 Hz, H-1); MS (EI, HR) m/z: found: 255.11031. Calcd for $C_{12}H_{17}NO_5$: 255.11067.

(2'R, 5'S) 4-*C*-(Clavamyl-2')-1,2-*O*-isopropylidene-3-*O*-methylthiomethyl-α-D-ribotetrofuranose (38); $[\alpha]_D$ 48.5 (*c* 0.1, CH_2Cl_2); IR ($CHCl_3$): 1780 cm^{-1}; ^1H NMR ($CDCl_3$): 1.36, 1.53 (2s, 6H, isopr.), 2.18 (s,

3H, SCH_3), 2.85 (dd, 1H, *J* 0.6, 16.2 Hz, H-6'a), 3.06 (ddd, 1H, *J* 0.8, 6.7 Hz, H-6a), 3.28 (ddd, 1H, *J* 0.9, 2.8, 16.2 Hz, H-6b), 3.94 (dd, 1H, *J* 7.0, 11.6 Hz, H-6b), 4.06 (dd, 1H, *J* 4.4, 9.1 Hz, H-3), 4.19 (dd, 1H, *J* 3.3, 9.1 Hz, H-4), 4.52 (dt, 1H, H-5), 4.68 (t, 1H, H-2), 4.69, 4.84 (2d, 2H, *J* 11.9 Hz, benzyl), 5.41 (d, 1H, *J* 2.8 Hz, H-5'), 5.79 (d, 1H, *J* 3.7 Hz, H-1); MS (EI, HR) m/z: M-15 found: 316.085623. Calcd for $C_{13}H_{18}NO_6S$: 316.08548.

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