Available online at www.sciencedirect.com
ScienceDirect
Carbohydrate Research 341 (2006) 2967–2972
Carbohydrate RESEARCH

Crystal and molecular structures of diglycosyl disulfide derivatives

Ivan Brito,[a] Matías López-Rodríguez,[b] Attila Bényei[c] and László Szilágyi[d,*]

[a]*Department of Chemistry, University of Antofagasta, Casilla 170 Antofagasta, Chile*
[b]*Instituto Universitario de Bio-Orgánica 'Antonio González', University of La Laguna, Astrofísico Francisco Sánchez N° 2, La Laguna, Tenerife, Spain*
[c]*Department of Physical Chemistry, University of Debrecen, H-4010 Debrecen Pf. 7, Hungary*
[d]*Department of Organic Chemistry, University of Debrecen, H-4010 Debrecen Pf. 20, Hungary*

Received 6 September 2006; received in revised form 13 October 2006; accepted 18 October 2006
Available online 25 October 2006

Abstract—The crystal and molecular structures of *S*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-*S*′-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)disulfide (**1**) and the mono-sulfoxide (**3**) of bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)disulfide (**2**) are described. Comparison of **2** and **3**, containing –S–S– and –S–S(O)– bonds, respectively, allows to delineate structural differences brought about by the different oxidation states of one of the sulfur atoms in carbohydrate disulfides.
© 2006 Elsevier Ltd. All rights reserved.

Keywords: Thiosulfinate; *S*-Oxide; Disulfide; Disaccharide; X-ray; Conformation

1. Introduction

The disulfide linkage plays an essential role in stabilizing tertiary structures of proteins and in many biologically relevant systems; it was, however, virtually nonexistent within carbohydrates of either synthetic or natural origin. This structural motif has recently been introduced into carbohydrate chemistry as a new interglycosidic connecting element and the synthesized *nonsymmetrical* diglycosyl disulfides were proposed as novel carbohydrate scaffolds with potential biological activity.[1,2] *Symmetric* disulfides formed through oxidation of 1-thioaldoses (see, e.g., Refs. 3 and 4) and some glycosyl-aryl/alkyl disulfides (see, e.g., Ref. 5) have, on the other hand, been known for a long time. Neoglycoconjugates bearing glycosyl units attached to proteins through S–S linkages represent another application of this bond type.[6–9]

The disulfide bond is an example of *three-bond interglycosidic linkages* (3BIGL: –X–Y–) incorporating two heteroatoms.[10] The shape of saccharide molecules, in general, is determined by the conformations around their glycosidic linkages. Three torsion angles, Φ, Ψ, and Ω are required to define the glycosidic conformation in 3BIGL structures (Chart 1).

A comparison of Ψ angles reported for various sugar derivatives with 3BIGLs shows[10] that the magnitude of this torsion is primarily dependent on the atoms interconnecting the two moieties of the molecules. The possibility to control molecular shapes in this way is of high importance to design molecules with predefined binding, and other, biological properties.

To our knowledge, very few crystal and molecular structures were published for carbohydrate disulfides, including the *symmetric* disulfides with (2,3:5,6-di-*O*-isopropylidene)-β-D-mannofuranosyl-[4] and 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl[11] (**2**) substituents. Here, we report on the crystal and molecular structures of two *nonsymmetrical* diglycosyl disulfide derivatives, the

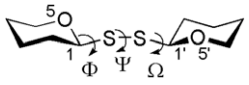

Chart 1. Definition of the interglycosidic torsion angles in 3BIGL structures. Φ: O5–C1–S–S; Ψ: C1–S–S–C1′; Ω: S–S–C1′–O5′.

* Corresponding author. E-mail: lszilagyi@tigris.unideb.hu

0008-6215/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.carres.2006.10.018

mono-sulfoxide[12] (**3**), obtained from **2**, and *S*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-*S*′-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)disulfide[1] (**1**).

2. Results and discussion

Mild oxidation of **2** with *m*-chloroperoxybenzoic acid (*m*-CPBA) furnishes a single oxidation product, which was tentatively assigned the thiosulfinate structure **3**.[12] No rigorous proof was, however, offered for this structure. Our X-ray data, to be discussed below, now provide firm evidence for the structure of **3**. On the other hand, comparison of **2** and **3** containing –S–S– and –S–SO– bonds, respectively, allows recognition of structural differences brought about by the different oxidation states of one of the sulfur atoms in saccharide disulfides.

We have reported the syntheses of several *nonsymmetrical* diglycosyl disulfide derivatives;[1] among these, compound **1** furnished crystals suitable for X-ray diffraction. The crystal and structure refinement data are listed in Table 1 while Table 2 summarizes selected bond lengths, bond- and torsion angles.

Inspection of the data in Table 2 shows that the structure of **1** (Fig. 1) is closely analogous to that of **2**,[11] which is not surprising. The disulfide torsion angle (C1–S1–S2–C21) is close to 90°, the value regularly observed in unrestricted acyclic disulfides.[13–15] Similar values have been reported from X-ray determination of alkyl-glycosyl disulfide structures with either furanosyl-[4] or pyranosyl[16] rings. Importantly, the helicity of the S–S-bond is *M* (Fig. 2).

This is, again, in agreement with the X-ray structures reported for symmetric (1,1′)-diglycosyl disulfide derivatives.[4,11] Inspection of molecular models indicate that the *P*-helical disulfide would bring the two glycopyranosyl rings closer resulting in a more crowded structure. This steric hindrance is relieved when at least one of the substituents of the disulfide bond is small, such as in alkyl-glycosyl disulfides, and either forms can occur. Indeed, the *S*–*S*-bond in methyl (2,3:5,6-di-*O*-isopropylidene)-β-D-mannofuranosyl-disulfide has a *P*-helicity,[4] whereas that of ethyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl-disulfide is *M*-helical[16] in the solid state. In solution both *M* and *P* forms can occur in equilibrium. Our preliminary NOE studies have, however, indicated

Table 1. Crystal data and structure refinement for **1** and **3**

Empirical formula	$C_{28}H_{38}O_{18}S_2$ (**1**)	$C_{28}H_{38}O_{19}S_2$ (**3**)
Formula weight	726.72	742.72
Temperature (K)	293	160(2)
Wavelength (Å)	0.71073	0.71073
Crystal system	Orthorhombic	Orthorhombic
Space group	$P2_12_12_1$ (No. 19)	$P2_12_12_1$ (No. 19)
Unit cell dimensions		
a (Å)	8.6532(10)	5.50(2)
b (Å)	13.9171(10)	22.22(8)
c (Å)	30.5871(10)	26.66(19)
α (°)	90.00	90.00
β (°)	90.00	90.00
γ (°)	90.00	90.00
V (Å^3)	3683.5(5)	3528(3)
Z	4	4
D_{calcd} (Mg m^{-3})	1.311	1.514
Absorption coefficient (mm^{-1})	0.217	0.249
F(000)	1528	1560
Crystal size (mm^3)	0.65 × 0.14 × 0.08	0.62 × 0.16 × 0.07
Crystal color	Colorless	Colorless
Habit	Needle	Prism
Theta range for data collection	2.46–25.3	2.30–25.3
Index ranges	$0 \leqslant h \leqslant 10$	$-6 \leqslant h \leqslant 6$
	$-5 \leqslant k \leqslant 16$	$-21 \leqslant k \leqslant 26$
	$0 \leqslant l \leqslant 36$	$-32 \leqslant l \leqslant 26$
Reflections collected	4020	15,885
Independent reflections	3748 [$R_{int} = 0.0047$]	5591 [$R_{int} = 0.064$]
Completeness of data	98%	96%
Absorption correction	Empirical (psi scan)	Multi-scan
Max/min transmission	0.7757/0.9828	0.953/0.983
Decay (%)	4%	None
Data/restraints/parameters	4020/0/433	5591/7/439
Final *R* indices [all data]	$R1 = 0.0897$, $wR2 = 0.1806$	$R1 = 0.0671$, $wR2 = 0.1549$
Goodness of fit on *F*2	1.084	1.104
Largest difference peak and hole	0.223/−0.212 (e Å^{-3})	0.620/−0.321 (e Å^{-3})

Table 2. Selected bond lengths (Å), bond- and torsion angles (deg)

	1	2[11]	3
S1–S2	2.025(5)	2.033(3)	2.137(8)
S1–C1	1.809(12)	1.802(7)	1.751(11)
S2–C21	1.798(11)	1.805(6)	1.793(9)
S2–O30	—	—	1.397(14)
C1–O1	1.426(11)	1.416(7)	1.374(9)
C5–O1	1.437(11)	n.a.	1.386(10)
C21–O21	1.435(11)	1.416(6)	1.425(8)
C25–O21	1.425(11)	n.a.	1.401(8)
C1–C2	1.515(15)	1.522(10)	1.532(9)
C21–C22	1.518(14)	1.527(8)	1.454(10)
O30–S2–S1	—	—	110.7(2)
C1–S1–S2	103.5(4)	103.9(2)	92.7(2)
C21–S2–S1	103.1(4)	104.2(2)	95.9(2)
S1–C1–O1	106.7(6)	108.6(4)	107.1(6)
O30–S2–C21	—	—	108.5(3)
S2–C21–O21	108.4(7)	109.4(4)	99.4(3)
S1–C1–C2	114.6(8)	115.4(4)	111.1(3)
S2–C21–C22	110.1(8)	109.8(5)	110.0(5)
O1–C1–C2	109.2(9)	108.8(5)	110.4(4)
O21–C21–C22	108.0	107.9	111.1
C1–S1–S2–C21	−83.4	−82.5	171.0
O1–C1–S1–S2	65.7	74.7	−73.9
O21–C21–S2–S1	−84.2	−87.2	−166.3
C2–C1–S1–S2	−55.3	−47.2	165.4
C22–C21–S2–S1	157.3	154.1	76.4
O21–C21–S2–O30	—	—	79.5

preponderance of the *M* form for nonsymmetrical (1,1′)-diglycosyl disulfides in solution too.[1] This observation was confirmed by recent circular dichroism measurements.[17] Pinto and co-workers[2] came to a similar conclusion for (1→4)-linked disulfide- and selenosulfide disaccharides. The C2–C1–S1–S2 and S1–S2–C21–C22 torsions indicate *syn* and *anti* geometry, respectively, the latter displaying more deviation from the ideal value (157° rather than 180°) just as in the symmetrical molecule **2**.[11] Accordingly, O21–C21–S2–S1 is −84.2°, significantly larger than O1–C1–S1–S2 (65.7°), which, itself, is close to the ideal gauche geometry. On the other hand, the S1–C1–C2 bond angle shows more distortion from tetrahedral than the corresponding S2–C21–C22 (114.6° vs 110.1°) again in close analogy with **2**.

Thiosulfinates, that is, mono-*S*-oxides of open chain disulfides have long been known[18] and the structures of some cyclic thiosulfinates have also been described (see, e.g., Refs. 19–21). Among carbohydrates, however, **3** has been the only known *S*,*S*′-diglycosyl thiosulfinate although its structure was not proved rigorously.[12] Very recently, Knapp et al. reported the formation of an analogous product upon oxidation of *S*,*S*′-bis(2-acetamido-3,4,6-tri-*O*-acetyl-α-D-glucopyranosyl)disulfide with *m*-CPBA[22] and the sulfoxide configuration of the product was tentatively assigned as *R*.[22] An interesting cyclic thiosulfinate was recently obtained as a single product by *m*-CPBA oxidation of a 1,6-disulfide-bridged hexopyranose[23] and its structure determined by X-ray crystallography. The sulfoxide configuration was found to be *S* in this derivative.[24]

Relevant structural parameters for **3** (Fig. 3) are listed in Table 2. A salient feature of thiosulfinates is that their *S*–*S*-bond is weaker than in disulfides.[18] Indeed, the *S*–*S*-bond in **3** is ca. 0.1 Å longer than in **1** or **2**. This figure as well as the *S*–*O* bond length and the S1–S2–O30 bond angle in **3** are comparable to the values recorded for aromatic-[18] and cyclic, noncarbohydrate thiosulfinates such as in 1,2-dithiane-[20] and 1,2-dithiolane[21] mono-sulfoxides as well as in the carbohydrate derivative referred to above.[24] Comparison with the X-ray structures reported for β-glycopyranosyl sulfoxides[25–28] reveals,

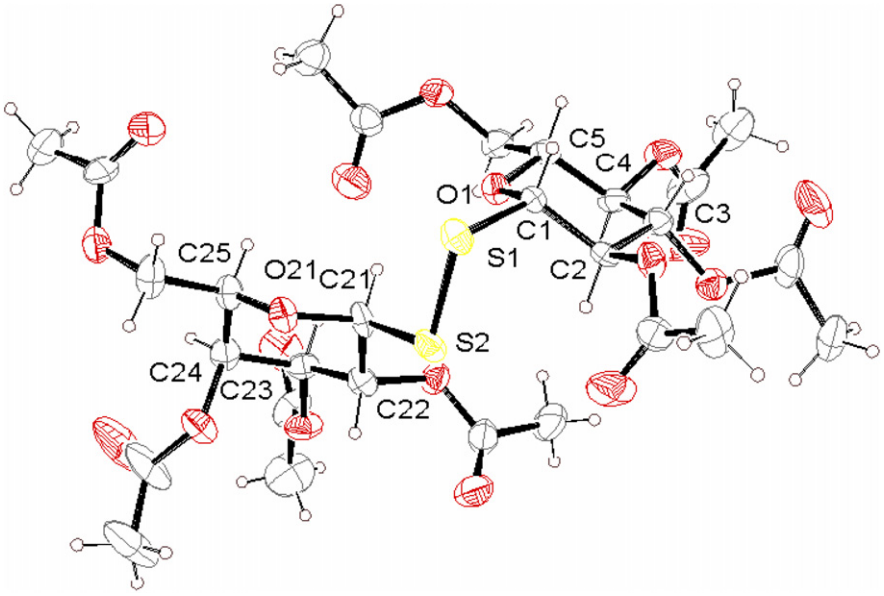

Figure 1. ORTEP plot of *S*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-*S*′-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)disulfide (**1**).

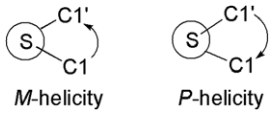

Figure 2. Definition of disulfide helicity.

however, significant differences (Table 2). Specifically, in **3** the S2–C21 (1.793 Å) and S2–O30 (1.397 Å) bond lengths are shorter, the S2–C21–O21 bond angle (99.4°) is smaller than in the reference sulfoxides; the average values in the latter being 1.838 Å, 1.489 Å, and 106°, respectively.

The sulfoxide configuration in **3** was found to be $(S)_S$ from the X-ray structure (Fig. 3 and Chart 2). In **3**, the C1–S1–S2–C21 torsion is 171°; this allows the pro-*S* lone pair of the divalent sulfur to occupy a quasi antiperiplanar position with respect to the *S–O* bond. This amounts to a rotation of the C21–S2 bond around the S1–S2 bond by ca. 90° from the quasi perpendicular arrangement, with respect to C1–S1, in the starting disulfide **2** (Fig. 4).

On the other hand, the O1–C1–S1–S2 torsion is changed from 74.7° in **2** to −73.9° in **3**, that is, flipped by ca. 150° around C1–S1. The sulfoxide is aligned to keep practically equal distances from the endocyclic C21–O21 as well as the exocyclic C22–O22 bonds of ring A as indicated by the respective angles (C21–O21/S–O: 79° and C22–O22/S–O: 88°).

The pyranosyl rings in both **1** and **3** adopt $^4C_1$ chair conformations with Cremer–Pople puckering parameters[29] as follow, **1**: $Q = 0.5560$(Glc) and 0.5725(Gal), $\theta = 6.84$(Glc) and 6.16(Gal); **3**: $Q = 0.5585$(ring A) and 0.5823(ring B), $\theta = 7.94$(ring A) and 12.04(ring B). The conformations of the acetyl groups are in agreement with the observation[30] that in acetylated pyranoses the carbonyl C═O bonds tend to align nearly eclipsing with the axial hydrogens on the ring carbons to which the acetoxy group is attached.

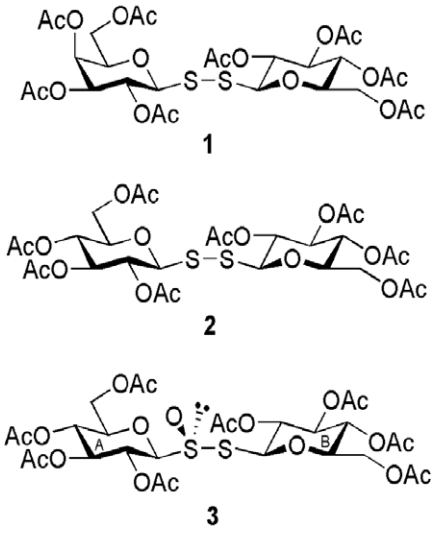

Chart 2. Sugar disulfide structures.

In summary, **1** and **2** are characterized by a compact structure with spatial proximity of the two pyranosyl rings, whereas in **3** these rings are kept apart resulting in a more open, extended structure. Changing the oxidation state of the sulfur therefore represents an important device to influence the conformations of 3BIGL disulfide sugars.

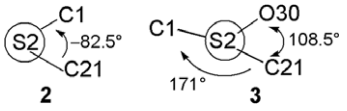

Figure 4. Relevant torsion angles in **2** and **3**.

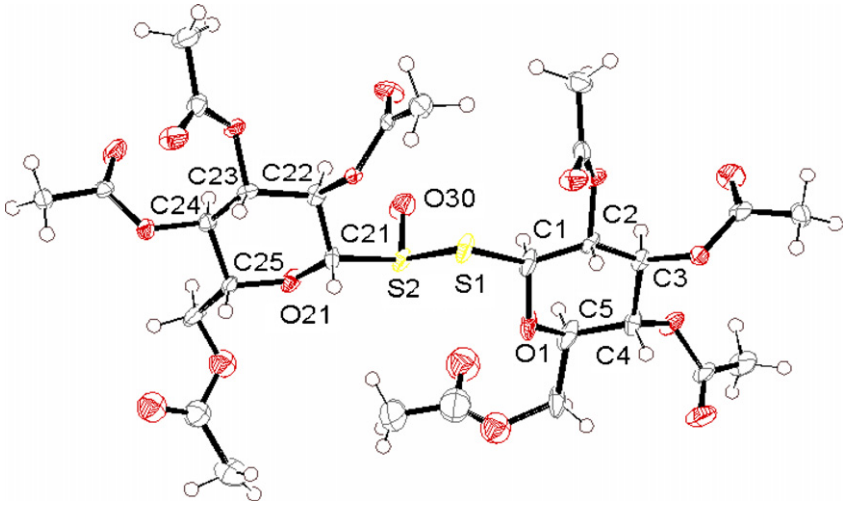

Figure 3. ORTEP plot of bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)disulfide mono-oxide (**3**).

3. Experimental

3.1. Materials

Compounds **1** and **3** were prepared by published procedures.

3.1.1. *S*-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-*S*′-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)disulfide (1).[1] Colorless crystals from EtOAc–hexane, mp: 163–164 °C, $[\alpha]_D$ 8.8 (*c* 1.84, $CHCl_3$); ^1H NMR (C_6D_6, 500 MHz): δ 5.73 (t, 1H, Gal-H-2); 5.62 (t, 1H, Gal-H-4); 5.60 (t, 1H, Glc-H-2); 5.40 (dd, 1H, Gal-H-3); 5.37 (t, 1H, Glc-H-4); 5.29 (t, 1H, Glc-H-3); 4.90 (d, 1H, Gal-H-1); 4.34 (m, 1H, Glc-H-6a); 4.26 (m, 1H, Gal-H-6a); 4.25 (d, 1H, Glc-H-1); 4.18 (m, 1H, Gal-H-6b); 4.10 (m, 1H, Glc-H-6b (t, 1H, Gal-H-5)); 3.32 (m, 1H, Glc-H-5). ^{13}C NMR (C_6D_6, 125 MHz): δ 89.16 (Gal-C-1); 86.15 (Glc-C-1); 76.29 (Glc-C-5); 74.56 (Gal-C-5); 73.88 (Glc-C-4); 71.83 (Gal-C-3); 68.98 (Gal-C-4); 67.61 (Gal-C-2, Glc-C-3); 67.11 (Glc-C-2); 61.03 (Glc-C-6); 60.77 (Gal-C-6).

3.1.2. Bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)disulfide mono-sulfoxide (3).[12] Colorless crystals from ethanol, yield: 40%, mp: 150–151 °C, $[\alpha]_D$ −51 (*c* 2.1, $CHCl_3$); $C_{28}H_{38}O_{19}S_2$ requires 742.150, *m/z* found: (ESI) $[M+Na]^+$ 765.139.

^1H NMR ($CDCl_3$, 500 MHz): δ 5.54 (t, 1H, H-2(A)); 5.35 (t, 1H, H-3(A)); 5.28 (t, 1H, H-3(B)); 5.19 (t, 1H, H-2(B)); 5.16 (t, 2H, H-4(A), H-4(B)); 5.01 (d, 1H, H-1(B)); 4.86 (d, 1H, H-1(A)); 4.29, 4.25, 4.21, 4.17 (m, 4H, H-6a6b(A), H-6a6b(B)); 3.85, 3.82 (m, 2H, H-5(A), H-5(B)). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 94.42 (C-1(A)); 83.94 (C-1(B)); 76.88, 76.63 (C-5(A), C-5(B)); 73.64, 73.24 (C-3(A), C-2(B)); 70.35 (C-3(B)); 67.58, 67.04 (C-4(A), C-4(B)); 65.49 (C-2(A)); 61.45, 61.38 (C-6(A), C-6(B)).

3.2. Single crystal X-ray experiments

X-ray quality crystals of **1** and **3** were fixed onto the tip of the glass fiber with epoxy glue. Data were collected at 160(2) K, Nonius KappaCCD area-detector diffractometer, Mo Kα radiation $\lambda = 0.71073$ Å, ω scans for **3** and, at 293(2) K, Enraf Nonius MACH3 diffractometer, Mo Kα radiation $\lambda = 0.71073$ Å, ω–2θ motion for **1**. The structures were solved using direct methods[31] and refined on F^2 using SHELX-97 program,[32] publication material was prepared with the WINGX-97 suite.[33] Absorption corrections were made either with multi-scan method SORTAV[34] (for **3**) or using the psi scan method[35] (for **1**). Crystallographic calculations were performed using the PLATON package.[36] Other details of X-ray structure determination are summarized in Table 1. Non-H atoms were refined anisotropically. C atoms of *O*-acetyl groups, together with C5 and C25, were refined isotropically for **3**; two *O*-acetyl groups (C5 and C25) are disordered over two sites with approx. 0.40:0.60 occupancies. In the final stage of refinement all hydrogen atoms were placed into geometric position using the riding model.

Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC Nos. 613462 and 613461 for compounds **1** and **3**, respectively. Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

Acknowledgements

These studies were supported by grants from the Hungarian National Science Fund, OTKA T48713 (to L.Sz.) and T43365 (to A.B.). I.B. thanks FONDECYT for Grant No. 1030052 and DGI (Universidad de Antofagasta) Grant No. 1345-02.

References

1. Szilágyi, L.; Illyés, T. Z.; Herczegh, P. *Tetrahedron Lett.* **2001**, *42*, 3901–3903.
2. Chakka, N.; Johnston, B. D.; Pinto, B. M. *Can. J. Chem.* **2005**, *83*, 929–936.
3. Staněk, J.; Šindlerova, M.; Černý, M. *Collect. Czech. Chem. Commun.* **1965**, *30*, 297.
4. Hürzeler, M.; Bernet, B.; Vasella, A. *Helv. Chim. Acta* **1992**, *75*, 557–588.
5. Bell, R. H.; Horton, D.; Miller, M. J. *Carbohydr. Res.* **1969**, *9*, 201.
6. Davis, B. G.; Lloyd, R. C.; Jones, J. B. *J. Org. Chem.* **1998**, *63*, 9614–9615.
7. Macindoe, W. M.; van Oijen, A. H.; Boons, G. J. *Chem. Commun.* **1998**, 847–848.
8. For a review, see: Davis, B. G. *Chem. Rev.* **2002**, *102*, 579–601.
9. Watt, G. M.; Boons, G. J. *Carbohydr. Res.* **2004**, *339*, 181–193.
10. For a review, see: Szilágyi, L.; Varela, O. *Curr. Org. Chem.* **2006**, *10*, 1745–1770.
11. Potrzebowski, M. J.; Michalska, M.; Błaszczyk, J.; Wieczorek, M. W.; Ciesielski, W.; Kaźmierski, S.; Pluskowski, J. *J. Org. Chem.* **1995**, *60*, 3139–3148.
12. Bell, R. H.; Horton, D. *Carbohydr. Res.* **1969**, *9*, 187–199.
13. Barltrop, J. A.; Hayes, P. M.; Calvin, M. *J. Am. Chem. Soc.* **1954**, *112*, 4348–4367.
14. Bergson, G. *Arkiv Kemi* **1962**, *18*, 409–434.
15. Guttenberger, H. G.; Bestmann, H. J.; Dickert, F. L.; Jorgensen, F. S.; Snyder, J. P. *J. Am. Chem. Soc.* **1981**, *103*, 159–168.
16. Grayson, E. J.; Ward, S. J.; Hall, A. L.; Rendle, P. M.; Gamblin, D. P.; Batsanov, A. S.; Davis, B. G. *J. Org. Chem.* **2005**, *70*, 9740–9754.

17. Kurtán, T.; Szilágyi, L.; Antus, S.; Illyés, T. Z., in preparation.
18. For a review, see: Lacombe, S. M. *Rev. Heteroatom. Chem.* **1999**, *21*, 1–41.
19. Juaristi, E.; Cruz-Sanchez, J. S. *J. Org. Chem.* **1988**, *53*, 3334–3338.
20. Seebach, D.; Beck, A. K.; Hayakawa, M.; Jaeschke, G.; Kuhnle, F. N. M.; Nageli, I.; Pinkerton, A. B.; Rheiner, P. B.; Duthaler, R. O.; Rothe, P. M.; Weigand, W.; Wunsch, R.; Dick, S.; Nesper, R.; Worle, M.; Gramlich, V. *Bull. Soc. Chim. Fr.* **1997**, *134*, 315–331.
21. Wu, S.; Greer, A. *J. Org. Chem.* **2000**, *65*, 4883–4887.
22. Knapp, S.; Darout, E.; Amorelli, B. *J. Org. Chem.* **2006**, *71*, 1380–1389.
23. Goddard-Borger, E. D.; Stick, R. V. *Aust. J. Chem.* **2005**, *58*, 188–198.
24. Goddard-Borger, E. D.; Skelton, B. W.; Stick, R. V.; White, A. H. *Aust. J. Chem.* **2005**, *58*, 199–205.
25. Buist, P. H.; Behrouzian, B.; MacIsaac, K. D.; Cassel, S.; Rollin, P.; Imberty, A.; Gautier, C.; Perez, S.; Genix, P. *Tetrahedron: Asymmetry* **1999**, *10*, 2881–2889.
26. Crich, D.; Mataka, J.; Zakharov, L. N.; Rheingold, A. L.; Wink, D. J. *J. Am. Chem. Soc.* **2002**, *124*, 6028–6036.
27. Showalter, H. D. H.; Winters, R. T.; Sercel, A. D.; Michel, A. *Tetrahedron Lett.* **1991**, *32*, 2849–2852.
28. Khiar, N.; Alonso, I.; Rodriguez, N.; Fernandez-Mayoralas, A.; Jimenez-Barbero, J.; Nieto, O.; Cano, F.; Foces-Foces, C.; Martin-Lomas, M. *Tetrahedron Lett.* **1997**, *38*, 8267–8270.
29. Cremer, D.; Pople, J. A. *J. Am. Chem. Soc.* **1975**, *97*, 1354–1358.
30. Perez, S.; Stpierre, J.; Marchessault, R. H. *Can. J. Chem.* **1978**, *56*, 2866–2871.
31. Altomare, A.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A. *J. Appl. Cryst.* **1993**, *26*, 343–350.
32. Sheldrick, G. M. SHELX97. Programs for Crystal Structure Analysis (Release 97-2). University of Göttingen, Germany, 1997.
33. Farrugia, L. J. *J. Appl. Cryst.* **1999**, *32*, 837–838.
34. Blessing, R. H. *J. Appl. Cryst.* **1997**, *30*, 421–426.
35. North, A. C. T.; Phillips, D. C.; Mathews, F. S. *Acta Crystallogr., Sect. A* **1968**, *24*, 351.
36. Spek, A. L. *J. Appl. Cryst.* **2003**, *36*, 7–13.