Dye-Sensitized Photooxygenation of 2,5-Bis(glycosyl)furans

Flavio Cermola*, Maria R. Iesce, Anna Astarita and Monica Passananti

Dipartimento di Chimica Organica e Biochimica Università di Napoli Federico II, Complesso Universitario di M. Sant'Angelo, Via Cinthia 4, 80126, Napoli, Italy

Received August 13, 2010: Revised December 29, 2010: Accepted March 25, 2011

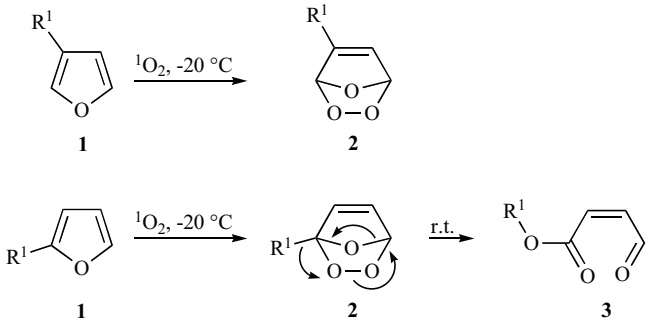
Abstract: The dye-sensitized photooxygenation of 2,5-bis(glycosyl)furans followed by warming up to r.t. provides 1,1'-linked disaccharides separated by a functionalized spacer. Asymmetrical disubstituted glycosyl furans give the corresponding Bayer-Villiger type-rearranged products in a molar ratio depending on the sugars and the protecting groups. The migratory aptitudes have been rationalized by both theoretical calculations and experimental data. The 1,1'-disaccharides obtained are new sugar derivatives structurally related to some mimetics of Sialyl Lewis X.

Keywords: [4+2]-Cycloaddition, endoperoxides, glycosyl furans, glycosides, photooxygenation, singlet oxygen, thermal rearrangement.

INTRODUCTION

Coupling reactions between a glycosyl-donor and an acceptor in the presence of a Lewis-acid as promoter represent the most general synthetic approach to glycosides. Many other pathways which make use of glycals as well as of lactone sugars are also useful synthetic routes [1]. Most of these procedures are based on the bond formation at the anomeric centre which represents the key step of the whole process. An alternative approach is based on building up the desired aglycone through selective and suitable reactions that are carried out on a pre-existent residue. Although this strategy is of less general use, it could be useful when coupling reactions could turn out unsuccessfully [1]. As part of our research program, we are investigating on the use of sugar-furans as building blocks for glycosides including functionalized frameworks, heterocycles or privileged structures as novel aglycones [2-5]. The approach is set up on a [4+2]-cycloaddition of singlet oxygen to diene function [6] of a glycosyl furan, e.g. **1**, followed by appropriate reactions on the related endoperoxide **2** (Scheme **1**). By this route, new glycosides [2, 3] and modified nucleosides [3-5] have been synthesized. It has also been found that the thermal stability of peroxides **2** is strictly dependent on the position of the sugar on the bicycle [2-6]. Indeed, while endoperoxides of 3-glycosyl furans are quite stable [4], those of 2-glycosyl furans by warming up to r.t. quantitatively rearrange to *O*-glycosides **3** through a Baeyer-Villiger mechanism-type that occurs with a complete retention of the configuration at the anomeric carbon (Scheme **1**) [2-6].

Continuing with this project, the present study deals with an investigation on the photooxygenation of novel 2,5-bis(glycosyl)furans in order to gain information on the thermal rearrangement of the corresponding 1,4-cycloadducts and verify the use of the procedure for new 1,1'-linked disaccharides separated by a functionalized spacer. These compounds are of interest because structurally related to mimetics of Sialyl Lewis X (sLe^X) [7], a tetrasaccharide which has been recognized to be involved in the initial step of inflammation response [7, 8]. Drug-design studies have evidenced that the biological activity of some of these mimetics is related to disaccharidic systems consisting of 1,1'-Gal-Man separated by a suitable spacer [8a].



Scheme 1.

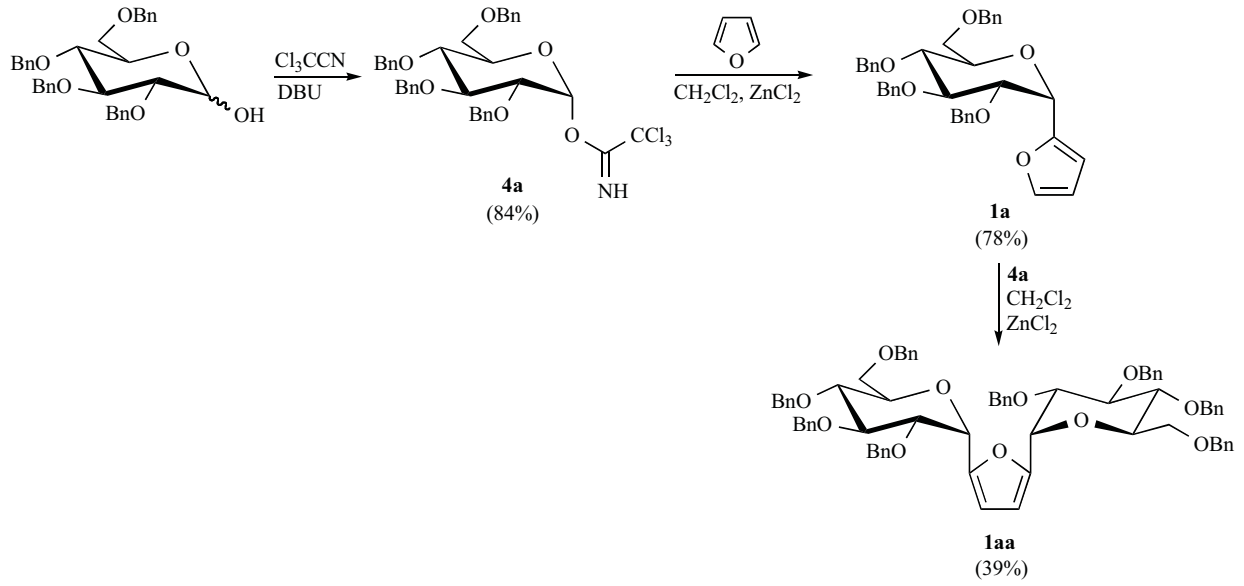
RESULTS AND DISCUSSION

Preliminarily, the reactivity of singlet oxygen towards 2,5-bis(2',3',4',6'-tetra-*O*-benzyl-D-glucopiranosyl)furan (**1aa**), chosen as model of a disubstituted sugar-furan, was examined. Furan **1aa** was synthesized following the pathway showed in Scheme **2** [9].

Owing to the high molecular symmetry, only one signal of the two anomeric protons appeared in the proton spectrum of **1aa** which authenticates the α-configuration at both the anomeric carbons [10]. The [4+2]-cycloaddition of singlet oxygen to **1aa** was performed in dichloromethane at -20 °C and, despite the high steric hindrance offered by the two sugar moieties, it was complete within 90 min (TLC). Then, the solution was transferred to r.t. and, after 10 min, analyzed by NMR spectroscopy. The ^1H spectrum of the crude mixture showed the quantitative formation of compound **3aa** that was spectroscopically characterized (Scheme **3**). In particular, according to the assigned

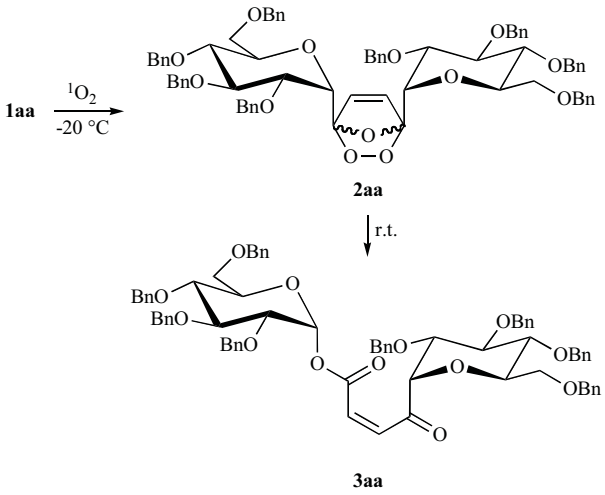
*Address correspondence to this author at the Dipartimento di Chimica Organica e Biochimica, Università di Napoli Federico II, Via Cintia 4, 80126 – Napoli, Italy; Tel: +39(0)81674331; Fax: +39(0)81674393;
E-mail: cermola@unina.it

1570-1786/11 $58.00+.00



Scheme 2.

structure, the signal of the anomeric proton of the migrated glucose is at δ 6.41, a typical value for the anomeric protons of *O*-glycosides [2-5].



Scheme 3.

Then, the asymmetrically disubstituted sugar-furans **1ab', 1ac'** and **1bc** were synthesized by using the α-**1b', α-1c'** and α-**1b** furans as glycosyl acceptors, respectively, and **4a** and **4c** as the donors (Scheme **4**) [11]. All of them were obtained as α-anomers at the newly formed stereocentres.

The three 2,5-bis(glycosyl)furans were photooxygenated in dichloromethane at -20 °C as above for **1aa**. After the completion of the reaction each crude mixture was transferred to r.t. and, after 10 min, spectroscopically analyzed. For **1ab'** the ^{1}H NMR spectrum showed the presence of the two disaccharides **3ab'-**GLU and **3ab'-**GAL in *ca.* 2 : 1 molar ratio, deriving from the diastereoisomeric endoperoxides **2ab'** by migration of the glucose and galactose unit, respectively (Scheme **5**). The reaction of **1ac'** afforded compounds **3ac'-**GLU and **3ac'-**MAN, in *ca* 6: 1 molar ratio (Scheme **5**).

Hence, the migratory aptitudes of the sugars in the thermal rearrangements of endoperoxides **2 ab'** and **2ac'** appeared to be glucose > galactose > mannose. However, photooxygenation of the bis(glycosyl)furan **1bc** afforded a mixture of the two derivatives **3bc-**GAL and **3bc-**MAN in ca. 1 : 1 molar ratio (Scheme **6**), suggesting that steric effects of the crowded protecting benzyl groups could have a role in promoting the rearrangement.

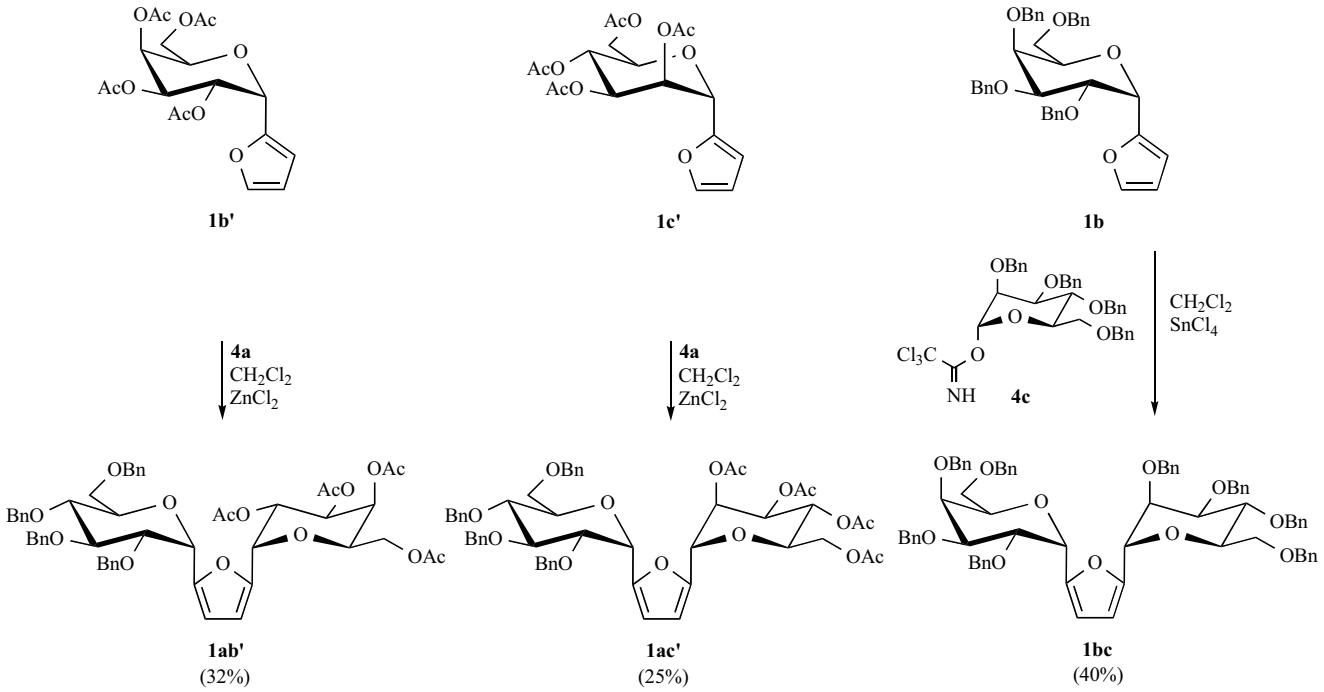
Theoretical calculations by MMFF models were carried out on acetylated glycosyl endoperoxides of monosubstituted furans **2a'**, **2b'** and **2c'**, chosen as models. They showed that the order of stability is **2a'** (Glu) < **2b'** (Gal) < **2c'** (Man) and fits with the observed migratory aptitude glucose > galactose > mannose (Fig. **1**) [12]. A possible explanation can be drawn by comparing the relationship between the groups at C-1 and C-2 and at C-1 and C-4 in the endoperoxide **2a'-c'**. These are *trans* (C1/C2) in the most stable **2c'**, *cis* (C1/C2) and *trans* (C1/C4) in **2b'** and all *cis* in the least stable **2a'** (Fig. **1**). The presence of encumbered protecting groups (e.g. benzyl group) exalts (e.g. in **2ab'** and **2ac'**) or overcomes (e.g. in **2bc**) these differences.

With the aim to support the steric control of the thermal rearrangement, we have synthesized and photooxygenated the glycosyl furans **1d** and **1e**, both α,α'-disubstitued with a benzylated glucose and with a benzyl and a trityl group, respectively (Scheme **7**).

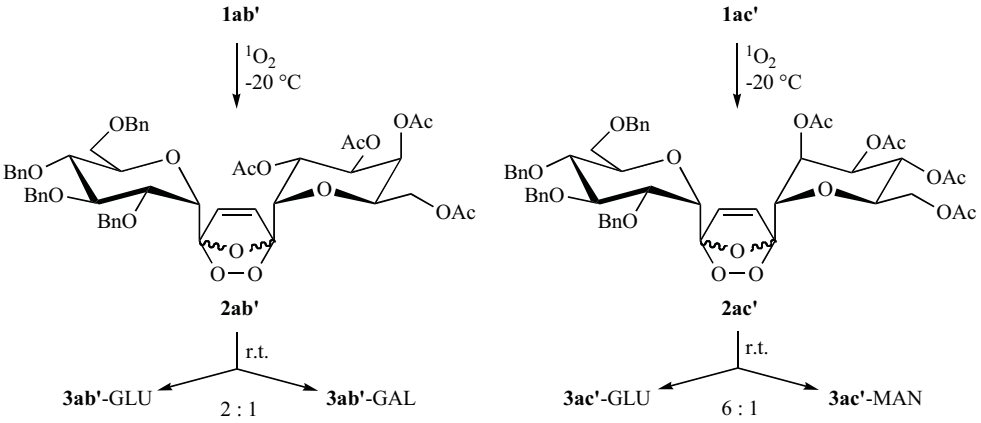
When the reactions were complete, each solution was transferred to r.t. and analyzed by ^{1}H NMR in C_6D_6 [13]. The spectra showed that for the endoperoxide **2d** only migration of the sugar occurs leading to **3d-**GLU, while **2e** leads to **3e-**GLU and **3e-**TRITYL in *ca*. 1 : 1 molar ratio, evidencing that migration of sugar competes with that of the particularly encumbered trityl group (Scheme **8**).

EXPERIMENTAL

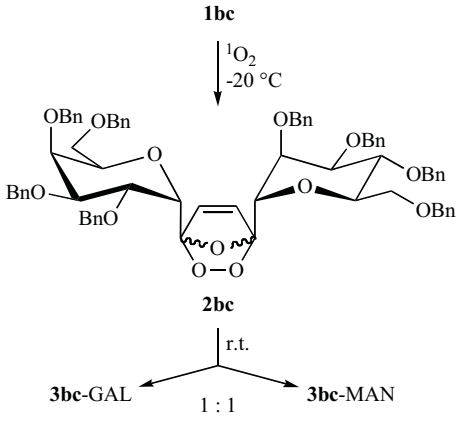
The spectra were recorded on the crude products at 500 MHz for [^{1}H] and 125 MHz for [^{13}C]. The carbons



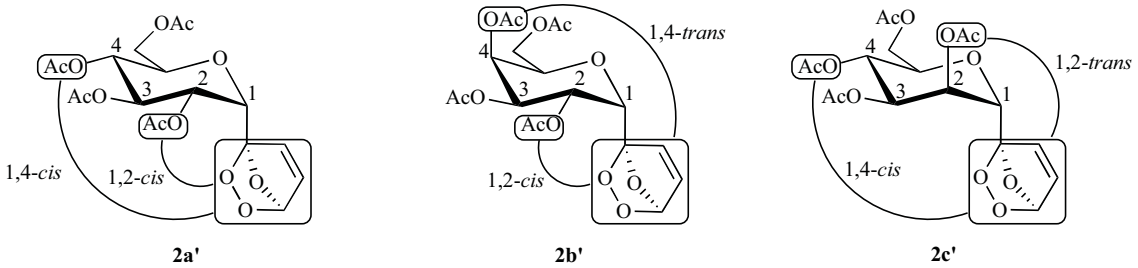
Scheme 4.



Scheme 5.



Scheme 6.



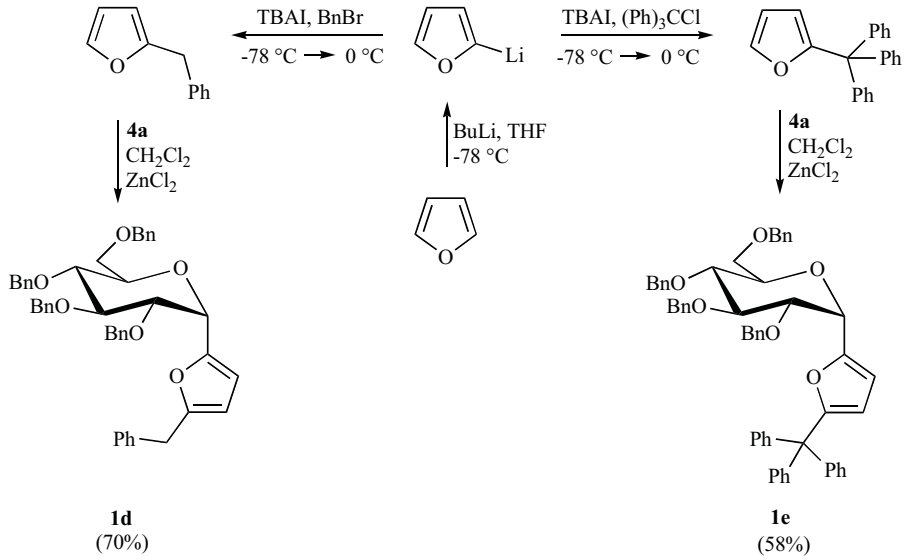
2a' **2b'** **2c'**

RR-**2a'** (341.61 KJ/mol) [*SS*-**2a'** (349.90 KJ/mol)]

RR-**2b'** (339.85 KJ/mol) [*SS*-**2b'** (347.65 KJ/mol)]

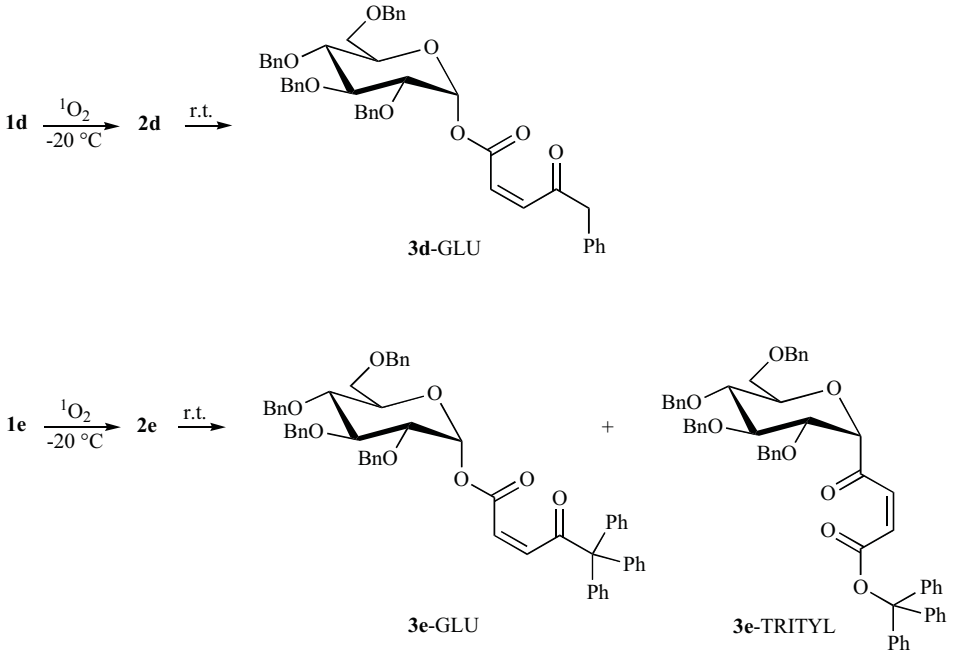
RR-**2c'** (336.18 KJ/mol) [*SS*-**2c'** (338.60 KJ/mol)]

Fig. (1). Interactions of C1/C2 and C1/C4 groups and energies of sugar endoperoxides **2a'**, **2b'** and **2c'** by MMFF models [12].



1d (70%) **1e** (58%)

Scheme 7.



3d-GLU **3e**-GLU **3e**-TRITYL

Scheme 8.

multiplicity was evidenced by DEPT experiments. The proton couplings were evidenced by ^{1}H-^{1}H COSY experiments. The heteronuclear chemical shift correlations were determined by HMQC (optimized for $^1J_{HC}$, 140 Hz) and HMBC (optimized for $^1J_{HC}$, 8 Hz) pulse sequences. The solvents used for the reactions were anhydrous. Reagent-grade commercially available reagents were used. Analytical TLC was performed on plates with 0.2 mm film thickness. Spots were visualized by UV light and by spraying with EtOH-H_2SO_4 (95: 5) followed by heating for 5 min at 110 °C. Silica gel (0063-0.2 mm), was used for column chromatography.

Synthesis of 2,5-bis(glucosyl)furan 1aa

To a stirred solution of 2,3,4,6-tetra-*O*-benzyl-glucopyranosyl-1-*O*-trichloroacetimidate (**4a**) (0.5 mmol) in dry CH_2Cl_2 (0.26 M) under argon and in the presence of molecular sieves, 2-(2',3',4',6'-tetra-*O*-benzyl-α-D-glucopyranosyl)furan (**1a**) (3 mmol) and, successively, a dichloromethane solution of $ZnCl_2$ (1 M, 2.6 mL) were added. The resulting mixture was stirred at room temperature for 24 h. The reaction was then quenched by saturated solution of $NaHCO_3$ (10 mL). The organic layer was separated and the aqueous layer was extracted with $CHCl_3$ (3 x 10 mL). The combined organic extracts were washed with brine and dried over anhydrous $MgSO_4$. After filtration the solvent was removed under reduced pressure. Silica gel chromatography using benzene/diethyl ether (9 : 1, v/v) as eluent afforded **1aa** in 35% yield.

1aa: oil; ^{1}H NMR ($CDCl_3$) δ= 3.45-3.64 (m, 6 H, H-5', H-6'$_a$, H-6'$_b$), 3.72 (m, 2 H, H-4'), 3.95 (dd, 2 H, *J*= 8.5, 6.4 Hz, H-2'), 4.28 (t, 2 H, *J*= 8.5 Hz, H-3'), 4.33 (d, 2 H, *J*= 12.1 Hz, C*H*$_2$Ph), 4.49 (2 d, 4 H, *J*= 11.6 Hz, C*H*$_2$Ph); 4.62 (s, 4 H, C*H*$_2$Ph), 4.79-4.82 (m, 4 H, C*H*$_2$Ph), 4.93 (d, 2 H, *J*= 11.6 Hz, C*H*$_2$Ph), 5.14 (d, 2 H, *J*= 6.4 Hz, H-1'), 6.50 (s, 2 H, H-3, H-4), 7.18-7.78 (m, 40 H, 8 C_6H_5); ^{13}C NMR ($CDCl_3$) δ= 68.3, 70.0, 72.3, 73.3, 75.1, 75.6, 77.9, 79.4, 83.1, 112.4, 127.0-129.0, 139.1, 139.2, 139.5, 139.7, 151.3. Anal. Calcd. For $C_{72}H_{72}O_{11}$: C, 77.67; H, 6.52. Found: C, 77.56; H, 6.43.

Synthesis of 1d

To a stirred solution of 2,3,4,6-tetra-*O*-benzyl-glucopyranosyl-1-*O*-trichloroacetimidate (**4a**) (0.5 mmol) in dry CH_2Cl_2 (0.26 M) under argon and in the presence of molecular sieves, 2-benzylfuran [14] (0.6 mmol) and, successively, a dichloromethane solution of $ZnCl_2$ (1 M, 2.6 mL) was added. The resulting mixture was stirred at room temperature for 4 h. The reaction was then quenched by saturated solution of $NaHCO_3$ (10 mL). The organic layer was separated and the aqueous layer was extracted with $CHCl_3$ (3 x 10 mL). The combined organic extracts were washed with brine and dried over anhydrous $MgSO_4$. After filtration the solvent was removed under reduced pressure. Silica gel chromatography using *n*-hexane/diethyl ether (9 : 1, v/v) as eluent afforded **1d** in 70% yield.

1d: oil; ^{1}H NMR ($CDCl_3$) δ= 3.53-3.70 (m, 4 H, H-4', H-5', H-6'$_a$, H-6'$_b$), 3.92 (dd, 1 H, *J*= 9.4, 6.0 Hz, H-2'), 3.97 (s, 2 H, C*H*$_2$Ph), 4.17 (t, 1 H, *J*= 9.4 Hz, H-3'), 4.45 and 4.58 (2 d, 2 H, *J*= 12.2 Hz, C*H*$_2$Ph), 4.50 and 4.80 (2 d, 2 H, *J*= 10.9 Hz, C*H*$_2$Ph), 4.64 (s, 2 H, C*H*$_2$Ph), 4.83 and 4.95 (2 d, 2 H, *J*= 10.9 Hz, C*H*$_2$Ph), 5.12 (d, 1 H, *J*= 6.0 Hz, H-1'), 5.94 (d, 1 H, *J*= 3.3 Hz, H-3), 6.46 (d, 1 H, *J*= 3.3 Hz, H-4), 7.22-7.78 (m, 25 H, 5 C_6H_5); ^{13}C NMR ($CDCl_3$) δ= 34.6, 68.8, 70.1, 72.7, 73.0, 73.4, 74.9, 75.5, 78.0, 79.6, 82.7, 106.8, 112.5, 126.4, 127.6, 127.7, 127.9, 128.3, 128.4, 128.7, 138.0, 138.1, 138.2, 138.4, 138.8, 149.4, 154.8. Anal. Calcd. For $C_{45}H_{44}O_6$: C, 79.39; H, 6.51. Found: C, 79.31; H, 6.48.

Synthesis of 1e

To a stirred solution of 2,3,4,6-tetra-*O*-benzyl-glucopyranosyl-1-*O*-trichloroacetimidate (**4a**) (0.5 mmol) in dry CH_2Cl_2 (0.26 M) under argon and in the presence of molecular sieves, 2-triylfuran [15] (0.6 mmol) and, successively, a dichloromethane solution of $ZnCl_2$ (1 M, 2.6 mL) was added. The resulting mixture was stirred at room temperature for 4 h. The reaction was then quenched by saturated solution of $NaHCO_3$ (10 mL). The organic layer was separated and the aqueous layer was extracted with $CHCl_3$ (3 x 10 mL). The combined organic extracts were washed with brine and dried over anhydrous $MgSO_4$. After filtration the solvent was removed under reduced pressure. Silica gel chromatography using *n*-hexane/diethyl ether (9 : 1, v/v) as eluent afforded **1e** in 58% yield.

1e: oil; ^{1}H NMR ($CDCl_3$) δ= 3.33-3.65 (m, 4 H, H-4', H-5', H-6'$_a$, H-6'$_b$); 3.92 (dd, 1 H, , *J*= 9.0, 5.6 Hz, H-2'), 4.05 (t, 1 H, *J*= 9.0 Hz, H-3'), 4.40 and 4.42 (2 d, 2 H, *J*= 12.0 Hz, C*H*$_2$Ph), 4.50 and 4.55 (2 d, 2 H, *J*= 11.9 Hz, C*H*$_2$Ph), 4.65 (s, 2 H, C*H*$_2$Ph), 4.70 and 4.78 (2 d, 2 H, *J*= 10.8 Hz, C*H*$_2$Ph), 5.09 (d, 1 H, *J*= 5.6 Hz, H-1'), 6.08 (d, 1 H, *J*= 3.0 Hz, H-3), 6.45 (d, 1 H, *J*= 3.0 Hz, H-4), 7.05-7.50 (m, 35 H, 7 x C_6H_5); ^{13}C NMR ($CDCl_3$) δ= 68.8, 70.0, 72.9, 73.4, 74.2, 74.8, 75.6, 77.7, 79.8, 82.9, 99.3, 111.4, 111.9, 126.5, 127.5, 127.6, 127.8, 127.9, 128.0, 128.1, 128.2, 128.3, 130.3, 138.1, 138.2, 138.3, 138.5, 138.8, 139.9, 150.9, 159. Anal. Calcd. For $C_{57}H_{52}O_6$: C, 82.18; H, 6.29. Found: C, 82.07; H, 6.20.

General Procedure of Dye-Sensitized Photooxygenation

A 0.02 M solution of furan **1** (0.25 mmol) in dry CH_2Cl_2 was irradiated at -20 °C with a halogen lamp (650 W) in the presence of methylene blue (MB, 1 x 10^{-3} mmol), while dry oxygen was bubbled through the solution. The progress of the reaction was checked by periodically monitoring the disappearance of starting material by TLC, or ^{1}H NMR. When the reaction was complete, the crude mixture was transferred to r.t. After 10 min, the solvent was removed under reduced pressure and the residue was filtered from diethyl ether to remove MB. After removal of diethyl ether, the residue was analysed by NMR spectroscopy.

Photooxygenation of 1aa

3aa: ^{1}H NMR ($CDCl_3$) δ= 3.58-3.84 (m, 10 H, H-6$_a$, H-6$_b$, H-4, H-5, H-2), 3.87 (t, 1 H, *J*= 7.7 Hz, H-3), 3.98 (t, 1 H, *J*= 8.2 Hz, H-3), 4.30 and 4.94 (2 d, 2 H, *J*= 12.0 Hz, C*H*$_2$Ph), 4.40-4.85 (m, 14 H, C*H*$_2$Ph), 4.94 (d, 1 H, *J*= 12.0 Hz, 7 C*H*$_2$Ph), 5.91 (d, 1 H, *J*= 12.2 Hz, C*H*=), 6.41 (d, 1 H, *J*= 3.6 Hz, H-1$_{O\text{-glu}}$), 6.58 (d, 1 H, *J*= 12.2 Hz, C*H*=), 7.10-

7.40 (m, 40 H, 8 C_6H_5). Anal. Calcd. For $C_{72}H_{72}O_{13}$: C, 75.50; H, 6.34. Found: C, 75.33; H, 6.22.

Photooxygenation of 1d

3d-GLU: ^{1}H NMR (C_6D_6) δ= 3.56 (dd, 1 H, , *J*= 7.4, 3.5 Hz, H-2), 3.60-3.78 (m, 4 H, CH_2Ph and H-6_a, H-6_b), 3.90 (t, 1 H, *J*= 7.4 Hz, H-3), 4.05-4.15 (m, 2 H, H-4 and H-5), 4.31 and 4.42 (2 d, 2 H, *J*= 12.0 Hz, CH_2Ph), 4.35 and 4.47 (2 d, 2 H, *J*= 11.0 Hz, CH_2Ph), 4.83 and 4.93 (2 d, 2 H, *J*= 11.5 Hz, CH_2Ph), 4.66 and 4.97 (2 d, 2 H, *J*= 12.0 Hz, CH_2Ph), 5.56 (d, 1 H, *J*= 12.4 Hz, C*H*=), 5.79 (d, 1 H, *J*= 12.4 Hz, C*H*=), 6.65 (d, 1 H, *J*= 3.5 Hz, H-1), 7.0-7.40 (m, 25 H, 5 x C_6H_5). Anal. Calcd. For $C_{45}H_{44}O_8$: C, 75.82; H, 6.22. Found: C, 75.69; H, 6.11.

Photooxygenation of 1e

3e-GLU and **3e-**TRITYL: ^{1}H NMR (C_6D_6) (selected signals) δ= 5.53 (d, 1 H, *J*= 11.9 Hz, C*H*= of **3e-**GLU), 5.71 (d, 1 H, *J*= 12.4 Hz, C*H*= of **3e-**TRITYL), 6.08 (d, 1 H, *J*= 11.9 Hz, C*H*= of **3e-**GLU), 6.32 (d, 1 H, *J*= 12.4 Hz, C*H*= of **3e-**TRITYL), 6.74 (d, 1 H, *J*= 3.6 Hz, H-1). Anal. Calcd. For $C_{57}H_{52}O_8$: C, 79.14; H, 6.06. Found: C, 79.01; H, 5.96.

CONCLUSION

The work has highlighted that the Bayer-Villiger rearrangement of endo-peroxides of 2,5-diglycosyl furans leads quantitatively to *O*-glycosides and depends on steric effects. In particular, the migratory aptitudes of the sugars depend on the stereochemistry of the chosen sugars and by the steric requirements of the protecting groups. Both theoretical and experimental data indicate that it is possible to drive the migration of a selected sugar by using suitable protecting groups.

Disaccharides 1,1'-linked by a spacer of 5 atoms have been obtained which are new sugar derivatives structurally related to some mimetics of Sialyl Lewis X. The efforts are now directed to achieve pure compounds **3** which will be deprotected and submitted to biological screening directed to highlight biological activity.

ACKNOWLEDGEMENTS

Financial support from the Ministero dell'Università e della Ricerca (MIUR, PRIN 2008) is gratefully acknowledged. NMR experiments were run at the Centro di Metodologie Chimico-Fisiche, Universita` di Napoli Federico II.

SUPPLEMENTARY MATERIAL

Supplementary material is available on the publishers Web site along with the published article.

REFERENCES

[1] Postema, H. D. M. *C-Glycoside Synthesis;* CRC Press: London, England, **1995**.

[2] Cermola, F.; Iesce, M. R.; Montella, S. The first dye-sensitized photooxygenation of 2-(*C*-glycosyl)furans. One-pot stereoselective approach to new carbohydrate derivatives, *Lett. Org. Chem.* **2004**, *1*, 271-275.

[3] Astarita, A.; Cermola, F.; Iesce, M. R.; Previtera, L. Dye-sensitized photooxygenation of sugar furans: novel bis-epoxide and spirocyclic *C*-nucleosides, *Tetrahedron* **2008**, *64*, 6744-6748.

[4] Cermola, F.; Iesce, M. R.; Buonerba, G. Dye-sensitized photooxygenation of furanosyl furans: synthesis of a new pyridazine *C*-nucleoside, *J. Org. Chem.* **2005**, *70*, 6503-6505.

[5] Cermola, F.; Iesce, M. R. Dye-sensitized photooxygenation of sugar-furans as synthetic strategy for novel *C*-nucleosides and functionalized exo-glycals, *Tetrahedron*, **2006**, *62*, 10694-10699.

[6] Iesce, M. R.; Cermola, F.; Temussi, F. Photooxygenation of heterocycles, *Curr. Org. Chem.,* **2005**, *9*, 109-139 and references therein.

[7] Kaila, N.; Thomas, B.E. Design and synthesis of Sialyl Lewis^x mimics as E- and P-selectin inhibitors, *Med. Res. Rev.* **2002**, *22*, 566-601 and references therein.

[8] a) Hiruma, K.; Kajimoto, T.; Weitz-Schmidt, G.; Ollmann, I.; Wong, C.-H. Rational design and synthesis of a 1,1-linked disaccharide that is 5 times as active as Sialyl Lewis X in binding to E-selectin, *J. Am. Chem. Soc.*, **1996**, *118*, 9265-9270; b) Cheng, X.; Khan, N.; Mootoo, D. R. Synthesis of the *C*-glycoside analogue of a novel Sialyl Lewis X mimetic, *J. Org. Chem*., **2000**, *65*, 2544-2547.

[9] The α-glucosyl furan **1a** used as the acceptor has been synthesized by a reported procedure: Schmidt, R. R.; Effenberger, G. *O*-Glycosyl imidates. 29. Reaction of *O*-(glucopyranosyl) imidates with electron-rich heterocycles. Synthesis of *C*-glucosides, *Liebigs Ann. Chem.* **1987**, *10*, 825-831.

[10] The coupling constant is the same of that of the 2-glucosyl furan **1a** ($^3J_{H1,H2}$= 6.4 Hz).

[11] It is used **a**, **b**, **c**, for benzylated glucose, mannose and galactose sugars, respectively, and **a'**, **b'**, **c'** for the corresponding acetylated ones. The acceptors **1b'**, **1c'** and **1b** were prepared by coupling between furan and the imidates **4b'**, **4c'** and **4b**, respectively. While **1c'** was obtainded only as α-anomer, **1b'** was formed as a α : β mixture in *ca.* 1 : 2 molar ratio, probably due to the neighboring-group participation of the acetyl at the C2 after the removal of the leaving group.

[12] Theoretical calculations were performed by SPARTAN '08 Quantum Mechanics Program.

[13] The NMR spectra were recorded in C_6D_6 to avoid also little extent of hydrolysis or *cis*/*trans*-isomerization of products which could be caused by the acidity of the $CDCl_3$.

[14] Wu, H.-J. and Lin, C.-C. First Exclusive Regioselective Fragmentation of Primary Ozonides Controlled by Remote Carbonyl Groups and a New Method for Determining the Regiochemistry of Carbonyl Oxide Formation, *J. Org. Chem*., **1996**, *61*, 3820-3828.

[15] 2-Tritylfuran has been prepared following the same procedure [14] used for 2-benzylfuran.