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ScienceDirect
Tetrahedron 62 (2006) 10694–10699
Tetrahedron

Dye-sensitized photooxygenation of sugar-furans as synthetic strategy for novel C-nucleosides and functionalized *exo*-glycals

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Received 5 June 2006; revised 26 July 2006; accepted 27 July 2006
Available online 18 September 2006

Abstract—The methylene blue-sensitized photooxygenation of β-ribofuranosyl furan **1e** followed by in situ Et_2S treatment afforded the conformationally stable β-ribofuranoside **4e** almost quantitatively. The latter was converted to pyridazine C-nucleoside **6e** by cyclization with NH_2NH_2 and to pyrazoline **7e** through a 1,3-dipolar cycloaddition with diazomethane. Attempts to epoxidize the double bond failed both by dimethyldioxirane (DMDO), which left **4e** unchanged, and by NEt_3/*t*-BuOOH or NaOO-*t*-Bu which respectively afforded the new and unexpected *exo*-glycals *E*,*Z*-**8e** and the novel furan derivative **9**.

1. Introduction and background

C-Glycoside synthesis represents a field of great interest due to the potential biological relationships, which often characterize these molecules.[1] Many synthetic approaches have been developed and others are being investigated for the purpose of furnishing more efficient procedures.[2] Two main synthetic pathways provide C-nucleosides as well as glycosides in general.[3] The most common approach is based on promoted coupling between a donor sugar and an acceptor, the latter being the desired aglycone.[2,3] The other approach involves transforming a suitable pre-existent aglycone by means of regio- and stereoselective reactions.[3] Although the first approach has wider applicability, it has definite limitations including isomerization or decomposition of the acceptor during the reaction due to the harsh conditions required. When this approach fails, the second strategy could represent the only possibility to achieve the target molecule.[3]

Furans are versatile and useful starting materials in the field of organic synthesis. For example, they are good diene-type compounds in [4+2] cycloaddition with singlet oxygen ($^1O_2$).[4] This excited state of oxygen can be easily produced starting from atmospheric oxygen, solar light and a sensitizer, which together constitute a reaction system of very low environmental impact. On the other hand, pericyclic reactions are known to proceed with very high regio- and stereoselectivity, the first of which fails when singlet oxygen is the dienophile,[5] as well as with good yields.[6] [4+2] Cycloaddition of singlet oxygen to furans has been applied with success in approaching highly functionalized molecules, which in turn can serve as building blocks in constructions of more complicated organic structures.[4] The reaction quantitatively affords 2,3,7-trioxabicyclo[2.2.1]hept-5-enes, usually named endoperoxides (Fig. 1),[4,5] which are thermally unstable. The rearrangement pathways strictly depend on the electronic nature of the substituents on the furan ring, providing useful approaches to a wide range of functionalized cyclic or acyclic compounds.[4,5,7]

Previous studies aimed at controlling dye-sensitized photooxygenation of furans bearing a sugar and investigated the reaction of glucosyl furans α-**1a**,**b** (Scheme 1).[8] The results showed that the sugar ring at the α-position of a furan strongly influences the chemical behaviour of the corresponding endoperoxides **2a**,**b**; they thermally rearranged into the corresponding α-O-glycosides **3a**,**b** through a Baeyer—Villiger-type mechanism (Scheme 1). This uncommon C- to O-glycoside transposition is promoted by the electrophilicity of the anomeric carbon and does not depend on the ring-sugar size. Indeed, similar results were obtained starting from the arabinosyl furans **1c**,**d**, which led quantitatively to the O-furanosides **3c**,**d** (Scheme 1).[9] Moreover, the use of the β-anomer of **1c** confirmed that the observed

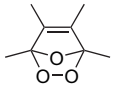

Figure 1. 2,3,7-Trioxabicyclo[2.2.1]hept-5-ene.

Keywords: Photooxygenation; [4+2] Cycloadditions; C-Nucleosides; 1,3-Dipolar cycloadditions.
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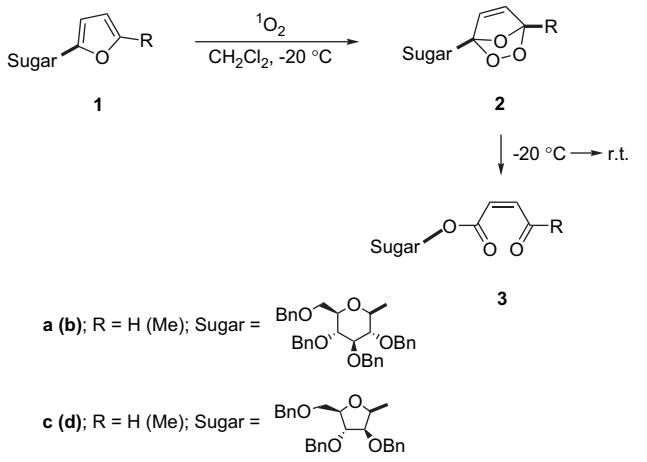
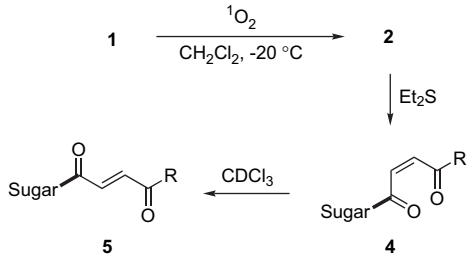
0040–4020/$ - see front matter © 2006 Published by Elsevier Ltd.
doi:10.1016/j.tet.2006.07.109

stereoselectivity is due to retention of the configuration in the sugar moiety from C- to O-migration (Scheme 1).[9]



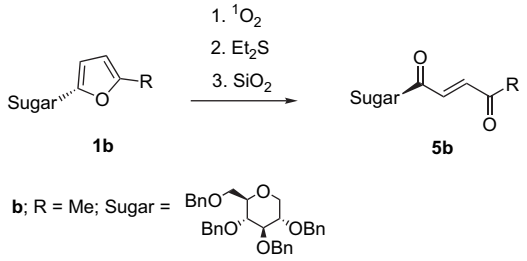
Scheme 1.

Although thermally unstable, the endoperoxides **2** could be used in approaching novel and functionalized C-glycosides. Indeed, when the photooxygenation mixtures of **2** were treated with a precooled (−20 °C) solution of Et_2S, the C-glycosides **4** were formed almost quantitatively (Scheme 2).[8,9] They were obtained with complete cis-stereoselectivity, owing to the bicyclic structure of the parent endoperoxides, but the use of chloroform or other slightly acid conditions promoted a complete isomerization into trans-derivatives **5** (Scheme 2).



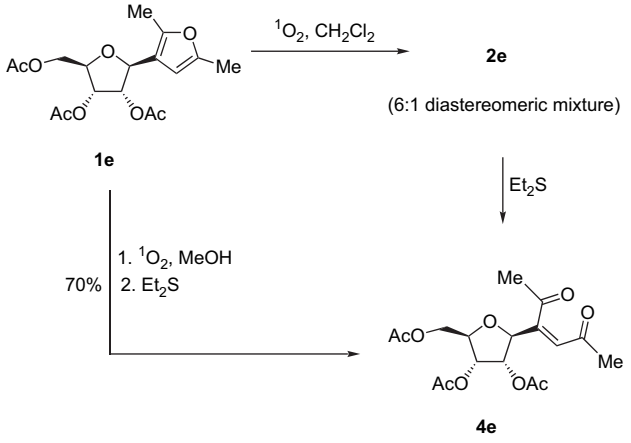
Scheme 2.

The development of the one-pot procedure shown in Scheme 3 is of considerable interest. It offers an easy synthetic approach for β-C-glycosides such as the derivative β-**5b**, starting from the corresponding α-glucosyl furans, for example, α-**1b**, which can be more easily prepared than the β-analogues.[8]



Scheme 3.

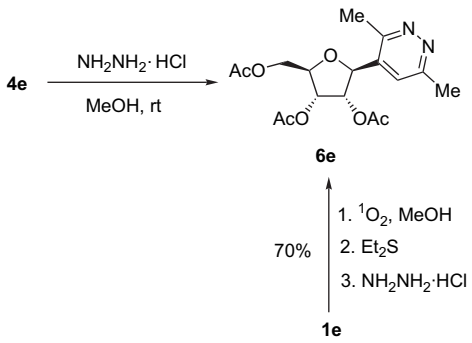
Subsequently, we decided to apply the photooxygenation procedure to β-ribofuranosides in the hope of producing novel C-nucleosides of pharmacological interest. Thus we synthesized the β-ribofuranosyl furan **1e**,[9] previously unknown, to obtain functionalized furanosides with configurationally stable unsaturated aglycones as well as to avoid the C- to O-rearrangement. The photooxygenation of β-**1e** in dichloromethane at −20 °C was complete after 30 min (TLC) and afforded the 6:1 diastereomeric mixture of the endoperoxide **2e**, which by Et_2S reduction quantitatively gave the *cis*-diketone **4e** (Scheme 4). As expected, compound **4e** showed a configurational stability, and did not isomerize at all into the corresponding *trans*-alkene.[9] Here we report some synthetic applications based on the use of the β-ribofuranoside **4e** as starting material for interesting new C-nucleosides and *exo*-glycals. Compound **4e** is easily prepared by a one-pot procedure based on the dye photooxygenation of the furanosyl furan **1e** followed by in situ Et_2S reduction (Scheme 4). Due to the high yield as well as the stereoselectivity, compound **4e** can be used without chromatographic purification.



Scheme 4.

2. Results and discussion

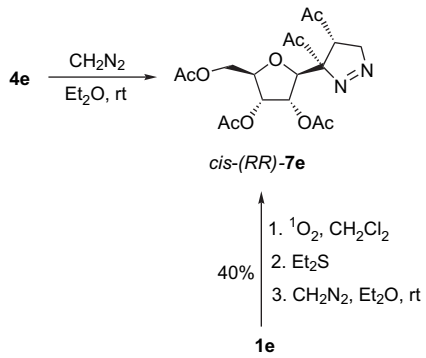
The cis-relationship of the two carbonyl groups of β-ribofuranoside **4e** and its configurational stability led us to carry out a cyclization into a pyrimidine-base system by the addition of hydrazine hydrochloride. The reaction was performed using dry methanol as the solvent and led to the new pyridazine C-nucleoside β-**6e** (Scheme 5). A one-pot process starting



Scheme 5.

from furan **1e** was then developed and afforded compound **6e** in 70% yield (based on furan **1e**).[9]

The presence of the peracetylated sugar ring as well as of two acetyl groups at the unsaturated carbons suggested the use of **4e** as a dipolarophile in [4+2] cycloadditions with electron-rich diene compounds as well as in [3+2] reaction with suitable 1,3-dipoles, providing six- and five-membered cyclic compounds, respectively. As 1,3-dipoles, diazoalkanes are usually able to give cycloadditions, which are HOMO-controlled by the dipole, the reactions proceeding faster with electron-poor alkenes.[10] Thus we chose diazomethane as the dipole and the reaction was carried out by adding an excess of a freshly prepared ether solution of CH_2N_2 to the ribofuranoside **4e** (0.5 mmol), while stirring at room temperature. After 30 min the reaction was complete (TLC), and the ^{1}H NMR spectrum showed the presence of an unknown derivative as the main product. On the basis of 2D-NMR experiments, we assigned the C-pyrazoline structure **7e** to the new product (Scheme 6).



Scheme 6.

The correctness of the assigned regiochemistry was easily established by the presence of the CH–CH_2 system in the ^{1}H NMR spectrum, which has to be absent in the regioisomer. The cis-facial relationship of the two acetyl groups was given on the basis of the concerted mechanism, which represents the usual pathway working in 1,3-dipolar cycloaddition reactions.[10] At present the configurations of the two new chiral centres have still to be assigned. Nevertheless, considering the cycloadducts similar to the transition states, we tentatively assigned the 4′*R*,5′*R* configurations to **7e**, on the basis of comparison of calculated thermodynamical stabilities of the two isomers. Indeed, a MM^+ conformational analysis assigned a lower energy to the *cis*-(*RR*)-**7e** of ca. 5 kcal/mol compared to the *cis*-(*SS*)-pyrazoline isomer **7e**′ (Fig. 2). All the spectroscopic data were collected on the crude reaction mixture, and this shows that the cycloaddition proceeds with very high yields and with almost complete regio- and stereoselectivity.

We next tested the possibility of oxidizing the double bond of **4e** using diverse epoxidizing reagents in order to achieve a new C-nucleoside characterized by an epoxidic aglycone. Treatment at −20 °C of a crude glycoside **4e** with freshly prepared dimethyldioxirane (DMDO) did not work, even after a week. This was only to be expected considering the electron-poor character of the double bond together with the electrophilicity of the oxidant.[11] We then attempted to epoxide the alkene moiety by using a *t*-BuOOH/NEt_3 mixture, a nucleophilic oxidizing system usually used in the epoxidation of alkenes substituted with two or three electron-withdrawing groups.[12] Unlike DMDO, the hydroperoxide/triethylamine solution generally leads to a mixture of *cis*- and *trans*-epoxides, the mechanism involved not being concerted.[12] The reaction was carried out by adding 6 equiv of the epoxidizing system to a stirred dichloromethane solution of **4e** at room temperature. Surprisingly, the work-up of the reaction after 12 h did not afford trace of any stereoisomeric epoxide; instead it produced the diastereomeric *exo*-glycals *E*,*Z*-**8e** in very high yields (Scheme 7). The molar ratio of *E*- and *Z*-**8e** changed from an initial 9:1 to 3:2 in the course of time.

The structure of *exo*-glycals for the two observed products was assigned on the basis of spectral data. The stereochemistry was firstly assigned by correlating the large differences in chemical shifts of the AB system protons of CH_2CO group to the different spacial closeness to the sugar chiral centres (ca. 0.5 ppm in *E*-**8e** vs 1 ppm in *Z*-**8e**). The assigned stereochemistry was then confirmed by 2D-NOESY experiments run on the diastereomeric mixture. In particular, the 2D-spectrum showed a strong NOE correlation between the methylene protons with the larger AB system and the

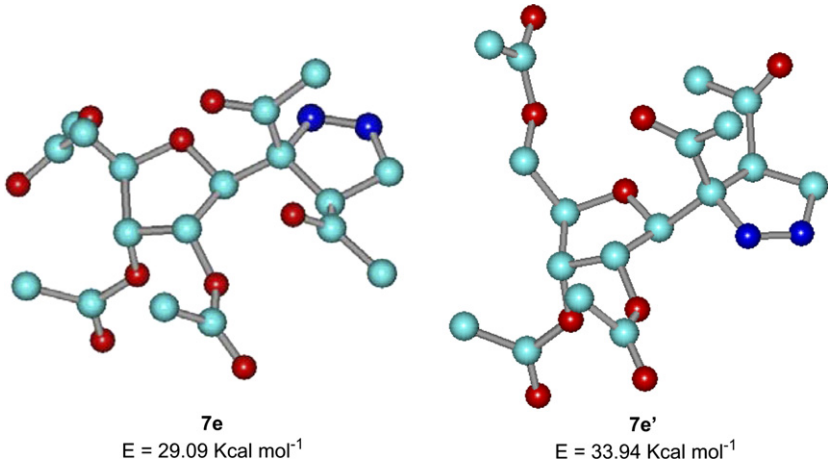
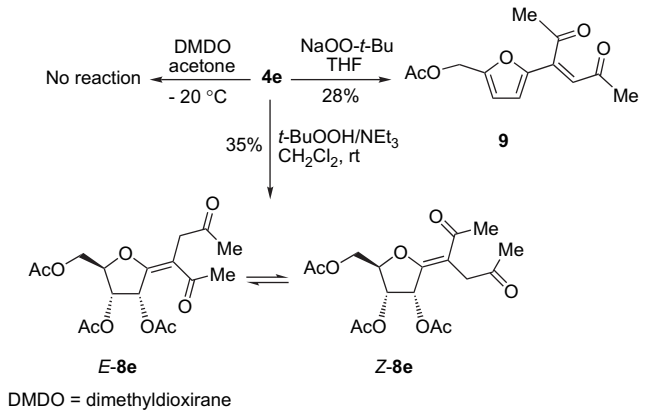


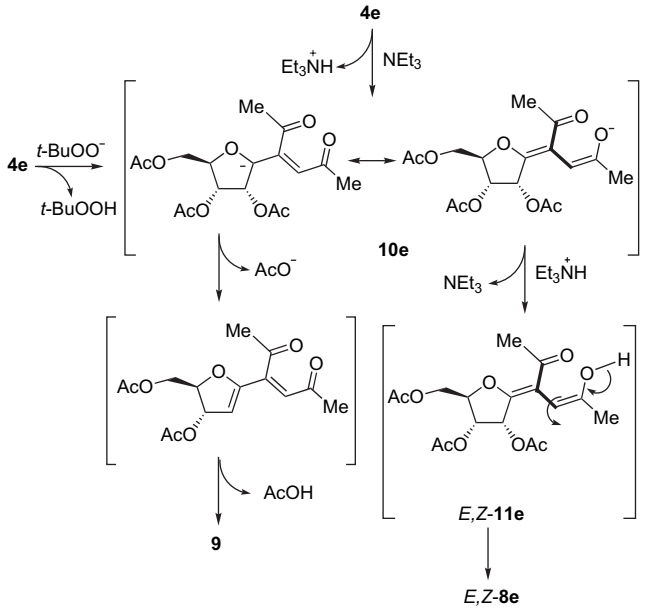
Figure 2. Conformational analysis (MM^+) for the *cis*-(*RR*)-**7e** and (*SS*)-**7e**′ pyrazolines.



Scheme 7.

doublet at δ 5.99 in agreement with the CH_2CO group at the same side of H-2, as occurs in the *Z*-configuration. Obviously, the same correlation was absent in the isomer *E*-**8e**.

This uncommon result shows that the acidity of the anomeric proton in **4e** is higher than that of the hydroperoxidic proton. This explains how triethylamine promotes the anion **10e** shown in Scheme 8. Due to the high conjugation of the system, subsequent re-protonation of the carbonyl oxygen should afford the undetected enol *E*,*Z*-**11e**, which tautomerizes into *Z*-**8e** and *E*-**8e**, the latter being initially the major isomer. The hypothesis was confirmed by control experiments. Indeed, when only NEt_3 was added to a solution of **4e**, compounds *Z*-**8e** and *E*-**8e** were the only products in the crude reaction mixture (^{1}H NMR).



Scheme 8.

The higher acidity of H-1 compared to *t*-BuOOH was demonstrated by the use of NaOO-*t*-Bu, freshly prepared by adding 1 equiv of NaH to the hydroperoxide at 0 °C in anhydrous THF.[13] With this reagent, the epoxidation reaction was still overcome by the acid–base reaction but surprisingly the furan **9** was formed (Scheme 7). The explanation may be that, due to the absence of an acid–base equilibrium, the fate of the anion **10e** is different from that previously observed in the presence of mild base NEt_3. It undergoes deacetylation of the sugar ring, the second elimination being very fast owing to the aromatization of the intermediate dihydrofuran system (Scheme 8).

It is noteworthy that deacetylation did not occur whether starting from furan **1e** or from 1,2,3,5-tetra-*O*-acetatyl-D-ribofuranose. Thus the electron-poor aglycone in **4e** should be responsible for the two observed reactions in that it increases the H-1 acidity, which represents the drawing force.

Although it was not possible to synthesize the planned epoxide, the above results illustrate the synthetic potential of the photooxygenation procedure applied to the sugar-furans **1**. They also highlight the high reactivity of unsaturated ribofuranoside systems such as **4e**, leading to a wide range of differently functionalized compounds, which in turn can be used as starting material for more complex glycosyl derivatives.

The synthesis of the new functionalized *exo*-glycals **8e** is of interest both for the potential biological activity[14] and for their synthetic application in producing pharmacologically active derivatives.[15]

Moreover, the work demonstrated the use of glycosides with α,β-unsaturated systems, such as compound **4e**, in [3+2] dipolar cycloadditions towards suitable 1,3-dipoles. This provides an easy access to C-nucleosides of pharmacological interest. Indeed, the reaction of **4e** with diazomethane leads regio- and stereoselectively to the novel pyrazoline C-nucleoside **7e**, which is structurally related to pyrazole C-nucleosides, compounds widely used for their pharmacological properties.[16]

3. Experimental

3.1. General

Nuclear magnetic resonance (NMR) spectra were recorded at 500 MHz for [^{1}H] and 125 MHz for [^{13}C] on a Fourier Transform NMR Varian 500 Unity Inova spectrometer. The carbon 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 and HMBC pulse sequences. ^{1}H–^{1}H proximities through space within a molecule were determined by NOESY. Analytical TLC was performed on precoated silica gel plates (Macherey-Nagel) with 0.2 mm film thickness. Column chromatography was performed on silica gel (Macherey-Nagel). Reagent-grade commercially available reagents and solvents were used.

3.1.1. Synthesis of 2′,5′-dimethyl-3′-(2,3,5-tri-*O*-acetyl-D-ribofuranosyl)furan β-1e. To a stirred solution of 2,3,5-tri-*O*-acetyl-1-*O*-(acetyl)-D-ribofuranose (320 mg, 1 mmol) in dry CH_2Cl_2 (10 mL) under argon and in the presence of molecular sieves 2,5-dimethylfuran (96 mg, 1 mmol) and, successively, a dichloromethane solution of $SnCl_4$ (1 M,

16 mL) were added. The resulting mixture was stirred at room temperature for 3 h. The reaction was then quenched by saturated solution of $NaHCO_3$ (5 mL). The organic layer was separated and the aqueous layer was extracted with $CHCl_3$ (3×10 mL). The combined organic extracts were washed with brine and dried over anhydrous $MgSO_4$. After filtration the solvent was removed under reduced pressure. ^1H NMR spectrum showed that glycosyl furan **1e** was present as a mixture of α and β-anomers in ca. 1:8 molar ratio.[17] Silica gel chromatography using *n*-hexane/EtOAc (85:15, v/v) as eluent afforded glycosyl furan β-**1c** in 35% yield: ^1H NMR ($CDCl_3$) δ 2.04 (s, 3H, CH_3CO_2), 2.10 (s, 6H, $2CH_3CO_2$), 2.20 (s, 3H, CH_3-2′), 2.24 (s, 3H, CH_3-5′), 4.21 (m, 2H, H-4 and H-5_A), 4.31 (dd, *J*=13.4, 4.6 Hz, 1H, H-5_B), 4.81 (d, *J*=7.0 Hz, 1H, H-1), 5.08 (dd, *J*=7.0, 5.7 Hz, 1H, H-2), 5.27 (dd, *J*=5.7, 4.1 Hz, 1H, H-3), 5.86 (s, 1H, H-4′); ^{13}C NMR ($CDCl_3$) δ 15.9 (q, CH_3-2′), 16.8 (q, CH_3-5′), 20.6 (q, CH_3CO_2), 20.7 (q, CH_3CO_2), 20.8 (q, CH_3CO_2), 63.8 (t, C-5), 71.7 (d, C-3), 74.8 (d, C-2), 75.2 (d, C-1), 79.6 (d, C-4), 104.2 (d, C-4′), 116.5 (s, C-3′), 148.4 (s, C-2′), 150.5 (s, C-5′), 169.6, 169.7 and 170.5 (3s, $3CO_2$).

3.1.2. One-pot synthesis of β-furanoside 4e by MB-sensitized photooxygenation of β-1e and Et_2S reduction. A 0.02 M solution of β-**1e** (0.25 mmol) in dry CH_2Cl_2 was irradiated at −20 °C with a halogen lamp (General Electric, 650 W) in the presence of methylene blue (MB, 1×10^{-3} mmol) while dry oxygen was bubbled through the solution. The progress of the reaction was checked by periodically monitoring the disappearance of **1e** (TLC or ^1H NMR). When the reaction was complete (90 min), a precooled dichloromethane solution of Et_2S (2 equiv) was added to the photooxygenation mixture. The latter was kept at −20 °C for 1 h and then transferred at room temperature. When the reduction was complete (2 h, ^1H NMR), the solvent and unreacted Et_2S were removed under reduced pressure. The residue was taken up in Et_2O, the suspension filtered to remove the insoluble sensitizer (MB) and the filtrate evaporated to give crude *cis*-β-**4e** (yield>90%). Silica gel chromatography on a short column gave pure compound **4e** in 70% yield.[9,18]

Compound **4e**: ^1H NMR ($CDCl_3$) δ 2.07 (s, 3H, CH_3CO_2), 2.08 (s, 3H, CH_3CO_2), 2.13 (s, 3H, CH_3CO_2), 2.26 (s, 3H, CH_3CO), 2.29 (s, 3H, CH_3CO), 4.14 (dd, *J*=12.1, 3.7 Hz, 1H, H-5_A), 4.20 (m, 1H, H-4), 4.35 (dd, *J*=12.1, 3.0 Hz, 1H, H-5_B), 4.60 (dd, *J*=6.0, 1.2 Hz, 1H, H-1), 5.22 (m, 2H, H-2 and H-3), 6.31 (d, *J*=1.2 Hz, 1H, H-3′); ^{13}C NMR ($CDCl_3$) δ 20.4 (q, CH_3CO_2), 20.5 (q, CH_3CO_2), 20.8 (q, CH_3CO_2), 30.5 (2q, $2CH_3CO$), 62.8 (t, C-5), 71.4 (d, C-3), 73.7 (d, C-2), 80.5 (d, C-4), 80.9 (d, C-1), 124.4 (d, C-3′), 153.9 (s, C-2′), 169.3 (s, CO_2), 169.6 (s, CO_2), 170.6 (s, CO_2), 196.5 (s, C-4′), 200.4 (s, C-1′).

In the subsequent reactions, crude *cis*-β-**4e** was used without further purification since control experiments showed that the presence of non-volatile Et_2SO was irrelevant.

3.1.3. Treatment of 4e with diazomethane. To the crude ribofuranoside **4e** (0.25 mmol) in dry Et_2O was added a diethyl ether solution of freshly prepared CH_2N_2 (ca. 1 mmol) and the resulting mixture was kept at room temperature under stirring. After 1 h the reaction was complete and the ^1H NMR showed the presence of pyrazoline **7e** as the only identifiable product (ca. 80%). After evaporation of the solvent, TLC chromatography of the residue (*n*-hexane/Et_2O, 1:4, v/v) afforded pure **7e** (50%; 40% based on starting furan **1e**).

cis-(*R*,*R*)-**7e**: ^1H NMR ($CDCl_3$) δ 2.06, 2.08, 2.14 (3s, 9H, $3CH_3CO_2$), 2.25 and 2.41 (2s, 6H, $2CH_3CO$), 3.26 (dd, *J*=8.8, 3.8 Hz, 1H, H-5′), 4.15 (m, 1H, H-4), 4.23 and 4.30 (2dd, *J*=12.6, 4.4, 3.3 Hz, 2H, H_2-5), 4.55 (dd, *J*=18.1, 8.8 Hz, 1H, H-$4'_A$), 4.67 (d, *J*=6.1 Hz, 1H, H-1), 4.76 (dd, *J*=18.1, 3.8 Hz, 1H, H-$4'_B$), 4.87 (t, *J*=6.1 Hz, 1H, H-2), 5.05 (dd, *J*=6.1, 5.5 Hz, 1H, H-3); ^{13}C NMR ($CDCl_3$) δ 20.5 (q, $2CH_3CO_2$), 20.8 (q, CH_3CO_2), 31.1 (q, CH_3CO), 32.4 (q, CH_3CO), 46.2 (d, C-5′), 62.5 (t, C-5), 70.5 (d, C-2), 71.2 (d, C-3), 79.8 (d, C-4), 81.6 (t, C-4′), 82.5 (d, C-1), 110.9 (s, C-1′), 169.1 (s, CO_2), 169.3 (s, CO_2), 173.4 (s, CO_2), 203.9 (s, CO), 208.0 (s, CO).

No other isomer was detected either by careful NMR analysis of the crude reaction mixture or by chromatography, and only polymeric material was found in addition to *cis*-(*R*,*R*)-**7e**.

3.1.4. Treatment of 4e with NEt_3/*t*-BuOOH.[12] Triethylamine (6 equiv) and *tert*-butyl hydroperoxide (6 equiv)[19] were added to a 0.1 M solution of crude ribofuranoside **4e** (1 mmol) in dry dichloromethane, and the resulting solution was kept at room temperature under stirring. When the reaction was complete (12 h, TLC), the mixture was partitioned between water and dichloromethane and the aqueous layer was extracted with further dichloromethane. The combined organic layers were then dried over Na_2SO_4. After evaporation of the solvents and unchanged reactants, the residue was chromatographed on silica gel eluting with *n*-hexane/AcOEt (2:3, v/v) and AcOEt, which afforded a mixture of *E*- and *Z*-**8e** in ca. 9:1 molar ratio, respectively (35%; 23% based on the starting furan). The ^1H NMR recorded on the same mixture kept at room temperature for 24 h showed that the molar ratio was changed to 3(*E*):2(*Z*).

E-**8e**: ^1H NMR ($CDCl_3$) δ 2.05, 2.08, 2.13, 2.16 and 2.20 (5s, 15H, $5CH_3CO$), 3.48 and 3.55 (2d, *J*=17.5 Hz, CH_2CO), 4.09 (m, 1H, H-5_A), 4.54 (m, 2H, H-4 and H-5_B), 5.37 (dd, *J*=8.2, 6.0 Hz, 1H, H-3), 6.31 (d, *J*=6.0 Hz, 1H, H-2); ^{13}C NMR ($CDCl_3$) δ 20.4 (q, CH_3CO_2), 20.5 (q, CH_3CO_2), 20.8 (q, CH_3CO_2), 28.7 (q, CH_3CO), 29.5 (q, CH_3CO), 41.5 (t, CH_2CO), 61.8 (t, C-5), 69.3 (d, C-2), 69.4 (d, C-3), 79.4 (d, C-4), 111.9 (s, C═), 162.3 (s, O–C═), 169.1 (s, CO_2), 169.3 (s, CO_2), 170.4 (s, CO_2), 196.7 (s, CO), 205.0 (s, CO).

Z-**8e** (in 2:3 mixture with *E*-**8e**): ^1H NMR ($CDCl_3$) δ 2.41 (s, 3H, CH_3CO), 3.22 and 3.33 (2d, *J*=17.5 Hz, CH_2CO), 4.25 (dd, *J*=12.4, 4.4 Hz, 1H, H-5_A), 4.54 (partially overlapped to the signal of *E*-**8e**, H-5_B), 4.75 (m, 1H, H-4), 5.26 (dd, *J*=8.1, 5.9 Hz, 1H, H-3), 5.99 (d, *J*=6.0 Hz, 1H, H-2); ^{13}C NMR ($CDCl_3$) δ 29.6 (q, CH_3CO), 31.9 (q, CH_3CO), 41.4 (t, CH_2CO), 61.1 (t, C-5), 69.0 (d, C-2), 70.3 (d, C-3), 81.7 (d, C-4), 111.7 (s, C═), 161.0 (s, O–C═), 169.2 (s, CO_2), 169.4 (s, CO_2), 170.3 (s, CO_2), 197.2 (s, CO), 205.7 (s, CO). The signals not reported are overlapped to those of *E*-**8e**.

3.1.5. Treatment of 4e with NEt_3. NEt_3 (1 equiv) in $CDCl_3$ (0.5 mL) was added to a solution of crude ribofuranoside **4e** in the same solvent (0.5 mL), and the resulting mixture was monitored by ^1H NMR. After 10 min, the spectrum showed the presence of the *E*- and *Z*-**8e** mixture in ca. 9(*E*):1(*Z*) molar ratio.

3.1.6. Treatment of 4e with NaOO-*t*-Bu.[13] A suspension of oil-free NaH (washed with hexane and dried) (50 mg, 2 mmol) in dry THF (20 mL) under the atmosphere of argon was cooled to 0 °C and 1.2 mL (6 equiv) of *t*-BuOOH (solution 5.0 M in decane) was added. The resulting mixture was warmed under stirring to 25 °C for 30 min, then cooled to 0 °C and a solution of the crude ribofuranoside **4e**, previously dried on P_2O_5 (95 mg, 0.25 mmol) in dry THF (10 mL), was added dropwise. The reaction mixture was stirred at 0 °C until the disappearance of compound **4e** (16 h, by TLC). Then, the solvents were removed under reduced pressure and the crude mixture was chromatographed on silica gel, using *n*-hexane/EtOAc (4:1) as eluent, to give furan **9** (28%; 22% based on the starting furan): ^1H NMR ($CDCl_3$) δ 2.11 (3H, s, CH_3CO_2), 2.32 and 2.47 (6H, 2s, $2COCH_3$), 5.07 (2H, s, CH_2), 6.48 (2H, br s, H-3 and H-4), 6.61 (1H, s, CH); ^{13}C NMR ($CDCl_3$) δ 20.5 (q, CH_3CO_2), 30.1 (q, CH_3CO), 30.9 (q, CH_3CO), 67.2 (t, CH_2), 114.2 (d, C-3), 116.2 (d, C-4), 118.9 (d, CH), 148.5 and 148.5 (2s, C-5 and C=), 152.1 (s, C-2), 169.3 (s, CO_2), 197.4 (s, CO), 202.6 (s, CO).

Acknowledgements

Financial support from MIUR (FIRB 2003–2005 and PRIN 2006–2008) is gratefully acknowledged. NMR experiments were run at the Centro di Metodologie Chimico-Fisiche, Università di Napoli Federico II.

References and notes

1. Simons, C. *Nucleoside Mimetics Their Chemistry and Biological Properties*; Gordon and Breach Science: Australia, Canada, 2001; (b) Peasley, K. *Med. Hypotheses* **2000**, *55*, 408.
2. See for example: Wu, Q.; Simons, C. *Synthesis* **2004**, 1533.
3. Postema, H. D. M. *C-Glycoside Synthesis*; CRC: London, 1995; (b) Du, Y.; Linhardt, R. J. *Tetrahedron* **1998**, *54*, 9913.
4. (a) Iesce, M. R.; Cermola, F.; Temussi, F. *Curr. Chem. Org.* **2005**, *9*, 109; (b) Matsumoto, M. *Singlet Oxygen*; Frimer, A. A., Ed.; CRC: Boca Raton, 1985; Vol. II, pp 205–272; (c) Bloodworth, A. J.; Eggelte, H. J. *Singlet Oxygen*; Frimer, A. A., Ed.; CRC: Boca Raton, 1985; Vol. II, pp 93–203.
5. Iesce, M. R. *Synthetic Organic Photochemistry*; Griesbeck, A. G., Mattay, J., Eds.; Marcel Dekker: New York, NY, 2005; Vol. 12, pp 299–363.
6. See for example: (a) Morgan, K. M. *Ann. Rep. Prog. Chem., Sect B: Org. Chem.* **2005**, *101*, 284; (b) Nicolaou, K. C.; Snyder, S. A.; Montagnon, T.; Vassilikogiannakis, G. *Angew. Chem., Int. Ed.* **2002**, *41*, 1668; (c) Wiest, O.; Houk, K. N. *Top. Curr. Chem.* **1996**, *183*, 1.
7. Scarpati, R.; Iesce, M. R.; Cermola, F.; Guitto, A. *Synlett* **1998**, 17; Gollnick, K.; Griesbeck, A. *Tetrahedron* **1985**, *41*, 2057.
8. Cermola, F.; Iesce, M. R.; Montella, S. *Lett. Org. Chem.* **2004**, *1*, 271.
9. Cermola, F.; Iesce, M. R.; Buonerba, G. *J. Org. Chem.* **2005**, *70*, 6503.
10. Regitz, M.; Heydt, H. *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley: New York, NY, 1984; pp 393–558.
11. Singh, M.; Murray, R. W. *J. Org. Chem.* **1992**, *57*, 4263.
12. Graziano, M. L.; Iesce, M. R.; Scarpati, R. *Synthesis* **1984**, 66.
13. Fernandez de la Pradilla, R.; Castro, S.; Manzano, P.; Martin-Ortega, M.; Priego, J.; Viso, A.; Rodriguez, A.; Fonseca, I. *J. Org. Chem.* **1998**, *63*, 4954.
14. For some recent examples, see: Lin, C.-H.; Lin, H.-C.; Yang, W.-B. *Curr. Top. Med. Chem.* **2005**, *5*, 1431; Stolz, F.; Reiner, M.; Blume, A.; Reutter, W.; Schmidt, R. R. *J. Org. Chem.* **2004**, *69*, 665; Tatibouet, A.; Rollin, P.; Martin, O. R. *J. Carbohydr. Chem.* **2000**, *19*, 641.
15. Taillefumier, C.; Chapleur, Y. *Chem. Rev.* **2004**, *104*, 263; Yang, W.-B.; Yang, Y.-Y.; Gu, Y.-F.; Wang, S.-H.; Chang, C.-C.; Lin, C.-H. *J. Org. Chem.* **2002**, *67*, 3773; Lay, L.; Nicotra, F.; Panza, L.; Russo, G.; Sello, G. *J. Carbohydr. Chem.* **1998**, *17*, 1269; Link, J. T.; Gallant, M.; Danishefsky, S. J.; Huber, S. *J. Am. Chem. Soc.* **1993**, *115*, 3782.
16. See for example Elgemeie, G. H.; Zaghary, W. A.; Amin, K. M.; Nasr, T. M. *Nucleosides Nucleotides Nucleic acids* **2005**, *24*, 1227; Nishiyama, Y.; Nishimura, N.; Kuroyanagi, N.; Maeba, I. *Carbohydr. Res.* **1997**, *300*, 183.
17. The β-anomer **1e** was the main product (β:α=8:1) owing to the neighbouring group of the acetyl at C-2 of the glycosyl donor.
18. Diacetylethylenes may undergo polymerization, mainly on contact with chromatographic adsorbents (Graziano, M. L.; Iesce, M. R.; Scarpati, R. *Synthesis* **1983**, 125).
19. High equivalents of the reactants were used to balance those oxidating diethyl sulfoxide present in the crude reaction mixture.