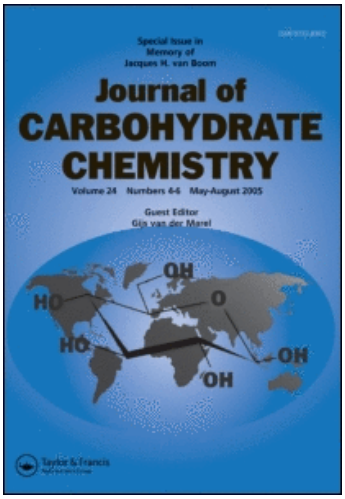

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Stereoselective Synthesis of [3.3.0]-Fused γ-Butyrolactones of Carbohydrates

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Stereoselective Synthesis of [3.3.0]-Fused γ-Butyrolactones of Carbohydrates†

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ABSTRACT

A facile and stereoselective method is described for the preparation of fused 2,3-γ-butyrolactones of lyxofuranose from the unexpected rearrangement in basic media of the photocycloadduct between homochiral 2(5*H*)-furanones and vinylene carbonate.

Key Words: Cyclobutanes; Stereoselection; Fused γ-butyrolactones; Lyxofuranose.

INTRODUCTION

The [2 + 2] photocycloaddition of alkenes to cyclic enones and α,β-unsaturated lactones is a well-known methodology to prepare cyclobutane compounds.[1] In the course of our ongoing research program in the stereoselective synthesis of natural occurring cyclobutane pheromones, we have studied the photocycloaddition of homochiral 2(5*H*)-furanones **1** to vinylene carbonate which lead to diastereo- and enantiomerically pure polyfunctionalyzed cyclobutane derivatives **2** (Scheme 1).[2,3] These

†This paper is dedicated to Professor Gérard Descotes on the occasion of his 70th birthday.

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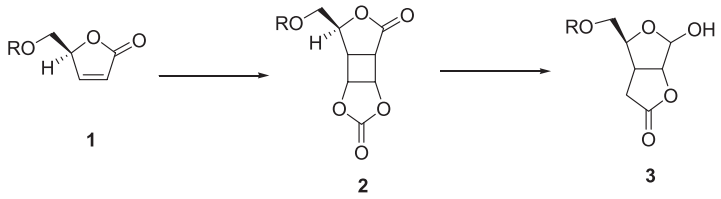

Scheme 1. Conversion of 2(5H)-furanones into fused 2,3-g-butyrolactones lyxofuranoses through a cyclobutane intermediate.

compounds could serve as useful precursors in asymmetric synthesis. When the resulting photocycloadduct **2** was subjected to dilute alkaline hydrolysis of the cyclic carbonate, an unexpected *cis* fused 2-*O*-3-*C*-γ-butyrolactone of lyxofuranose **3** was obtained in a highly stereospecific manner.[4]

Fused [3.3.0] lactones (γ-butyrolactones) of carbohydrates are convenient synthons for the preparation of branched chain sugars and nucleosides through ring opening of the lactone moiety.[5–7] *C*-branched nucleosides bearing carbon-carbon bonds at the furanose ring have attracted considerable attention because of the wide range of biological activity displayed by these products: antitumoral, antiviral and antibacterial activity.[8] Synthesis of fused γ-butyrolactones at the 2,3 position of the ribofuranose ring have already been reported.[9,10] However, to the best of our knowledge, examples of fused 2,3-γ-butyrolactones at the lyxofuranose ring have not yet been described. Moreover, such bicyclolactones are considered good candidates for a solution to the off-template problem of carbohydrate natural product synthesis by the creation of a new chiral center at the α-carbon of the butyrolactone which was not part of the original carbohydrate template.[11,12] Consequently, we felt it would be of interest to study the scope of the above process as a practical synthetic method. Herein, we describe full details of our results directed toward the diastereoselective preparation of the photoadducts and its application to the synthesis of fused 2,3-γ-butyrolactones of carbohydrates.

RESULTS AND DISCUSION

The 2(5*H*)-furanones **4a–c** (Figure 1), differently substituted at C-2 and C-3 (R_1 = H, CH_3; R_2 = H, CH_3), were chosen as convenient substrates to gain some insight into the formation of the γ-butyrolactones. The pivaloyloxymethyl group has recently proved quite efficient in inducing facial discrimination on the photocycloaddition to ethylene and acetylene and it was selected as an appropriate protecting group of the primary hydroxyl.[13]

Lactone **4a** was easily prepared in 89% yield by the reaction of (*S*)-5-hydroxymethyl-2(5*H*)-furanone with pivaloyl chloride, DMAP and pyridine in CH_2Cl_2.[14] The 3-methyl derivative **4b** was synthesized in 70% yield by a two step protocol: 1,3-dipolar cycloaddition of CH_2N_2 to **4a** in ether, followed by pyrolysis of the corresponding pyrazoline in dioxane.[2,3] The new furanone **4c** was prepared from **4a** in 46% yield through a sequence that involves cycloaddition-methylation-cycloreversion as

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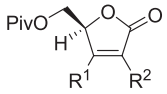


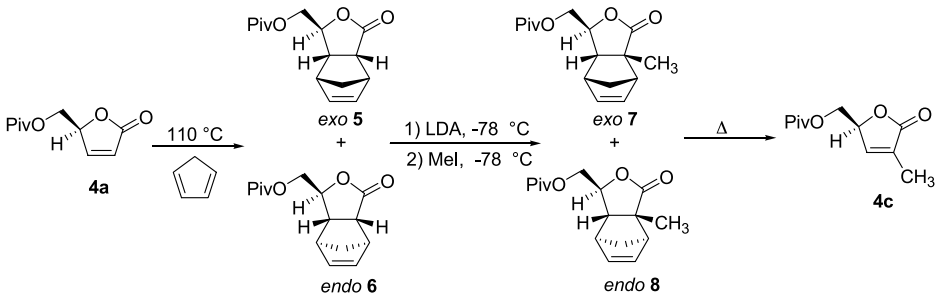
4a $R^1 = H$; $R^2 = H$
4b $R^1 = CH_3$; $R^2 = H$
4c $R^1 = H$; $R^2 = CH_3$

Figure 1. 2(5H)-furanones used as photochemical substrates.

outlined in Scheme 2.[15] Thus, reaction of **4a** with a large excess of cyclopentadiene, at 110°C for 19 h and in the presence of hydroquinone, afforded in 81% yield an 85:15 mixture of the *endo* and *exo* cycloadducts, **5** and **6**. For characterization purposes, both adducts were isolated by flash column chromatography, but separation was not necessary for further synthetic transformations. α-Methylation was accomplished in 80% yield by treating the mixture of the *endo-exo* cycloadducts with 2 equiv of LDA and an excess of MeI. Finally, a mixture of the resulting compounds **7** and **8** was submitted to pyrolysis at 250°C for 6 days to afford the expected lactone **4c** in 71% yield.

Next, we studied the photochemical reaction of lactones **4a–c** with vinylene carbonate (Scheme 3). Thus, substrates **4a–c** with a five molar excess of vinylene carbonate in acetone were irradiated through a pyrex filter with a medium pressure 125W mercury lamp at −78°C. With the exception of **4c**, two isomeric cycloadducts derived from an *exo* approach of the olefin to the furanone ring were obtained. The results are listed in Table 1.

The diastereomers were separated by flash column chromatography and their structures were established by detailed analyses of their ^1H and ^{13}C NMR spectra. When $R_1 = H$, the *anti*/*syn* stereochemistry was elucidated considering the value of the coupling constant between H-4 and H-5; the *anti* isomers **10a**,**c** showed a small $J_{4,5}$ (around 1.5 Hz), while the *syn* isomer **11a**,**c** had a larger $J_{4,5}$ (around 6.0 Hz). When $R_1 = Me$, the *anti*/*syn* configuration was determined by the chemical shift of the angular methyl carbon on the ^{13}C NMR spectrum. The ''steric compression'' in the *anti* adduct is much larger than in the *syn* one, therefore the signal of the methyl carbon



Scheme 2. Preparation of 4c.

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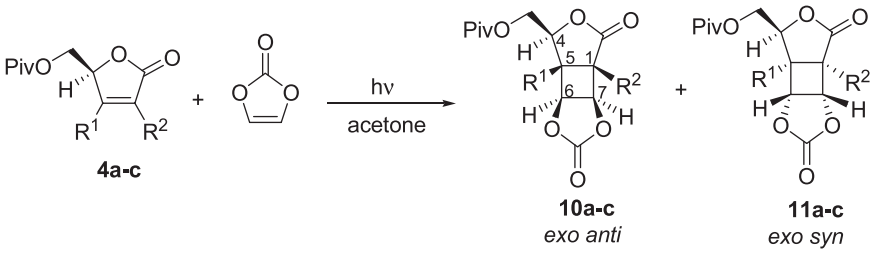

Scheme 3. Photocycloadditions with vinylene carbonate.

in the former diastereomer **10b** appears high field shifted (δ 16.4 ppm) when compared with the latter adduct **11b** (δ 20.1 ppm). The *exo* arrangement was inferred from the values of the vicinal coupling constants $J_{1,7}$ (0–1.2 Hz) and $J_{5,6}$ (1.8–2.9 Hz).

The diastereofacial differentiation of these photocycloadditions was consistent with a preferential *exo* approach of the cyclic carbonate to the least hindered face of the furanone, giving the *exo-anti* isomers as the major products. Accordingly, the *anti*:*syn* ratio ranges from 86:14 for lactone **4a** (entry 1) to 88:12 for lactone **4b** (entry 2).[2,3] Furthermore, for lactone **4c** the *syn* cycloadduct was not detected (entry 3). The ^{1}H and ^{13}C NMR spectra of the reaction mixture showed a main set of signals, which were assigned to the *anti* cycloadduct, along with other minor signals that could not be attributable to the *syn* cycloadduct. The high selectivity accomplished in this case suggests that the α-methyl group is indeed extremely important in directing the stereochemical outcome of the photoreaction. The results obtained can be rationalized on the basis of the influence that both steric and electronic factors exert on the orientation of the furanone diastereotopic face and the attacking olefin.

Once with the cyclobutane derivatives in our hands, we decided to explore the preparation of the γ-butyrolactones by submitting the *anti* cycloadducts to basic conditions. Firstly, treatment of the cycloadduct **10a** with 0.5 M NaOH in a mixture of water and dioxane (1:1) for 30 min, resulted in the formation of the *cis* fused 2,3-butyrolactone of lyxofuranose **12a** in 33% yield (Figure 2, Table 2). Similar results came out for cycloadducts **10b**,**c**, affording the γ-butyrolactones **12b**,**c** in 30% and 28% yield, respectively (entries 2 and 3). It was found, however, that improved yields (44–50%) of **12a–c** could be obtained by using a catalytic amount of MeONa in MeOH (entries 4–6).

Table 1. Photocycloaddition of lactones **4a–c** to vinylene carbonate.

Entry	2(5*H*)-furanone	Time	Yield[a]	**10***anti*:**11***syn*[b]
1	**4a**	4h	50%	86:14
2	**4b**	6h	54%	88:12
3	**4c**	6h	61%	100:-

[a]Isolated yield after column chromatography purification.
[b]Ratio of isolated products.

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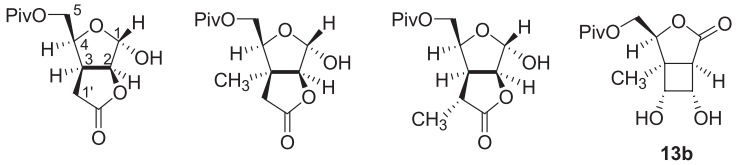

Figure 2. [3.3.0]-fused g-butyrolactones of lyxofuranose synthesized.

Structures of all new compounds were assigned unequivocally on the basis of the corresponding spectroscopic data, using a combination of ^{1}H-^{1}H COSY, HMBC-2D and ^{1}H-^{13}C HETCOR experiments. All compounds show similar $J_{1,2} = 0$ Hz and $J_{2,3} \approx 7.0$ Hz values in the ^{1}H NMR spectra. In compound **12c**, a new stereogenic center is created at the ''off template'' site of the furanose ring with complete diastereoselectivity. The absolute stereochemistry at the newly formed stereocenter was determined by NOE experiments. Thus, irradiation of the H-1′ proton caused enhancement of the signal of protons H-5a,b (4%), indicating that the configuration at C-1′ was (*R*). A plausible mechanism that accounts for the stereospecific formation of the γ-butyrolactones and the stereochemical outcome of the rearrangement has been reported by us in a previous communication.[4]

At this point, it seemed interesting to submit the *syn* cycloadducts, which should lead to γ-fused butyrolactones of ribofuranoside, to the same experimental conditions. Unfortunately, these cycloadducts showed a completely different behavior. Thus, under the foregoing conditions compound **11a** underwent decomposition to unidentified products, while **11b** gave the diol **13b** by hydrolysis of the cyclic carbonate. These results show that configurations at the cyclobutane moiety of the cycloadducts have a remarkable effect on this type of rearrangement.

In summary, we have achieved a stereoselective synthesis of a series of γ-butyrolactones of lyxofuranose in moderate yields by the rearrangement of the readily available *anti* photoadducts between homochiral 2(5*H*)-furanones and vinylene carbonate. Using an α-substituted furanone, a new chiral center is formed at the ''off template'' site of the lyxofuranose ring, with excellent diastereoselectivity. These γ-butyrolactones of sugars described above can be considered as useful chiral synthons for the preparation of 3-*C*-branched chain sugars and nucleosides. Active investigation in this field is being carried out in our laboratory and will be described in due course.

Table 2. Stereoselective rearrangement of the *anti* cycloadducts to γ-butyrolactones.

Entry	Cycloadduct	Method	γ-Butyrolactone	Yield
1	**10a**	$NaOH/H_2O$/dioxane	**12a**	33%
2	**10b**	$NaOH/H_2O$/dioxane	**12b**	30%
3	**10c**	$NaOH/H_2O$/dioxane	**12c**	28%
4	**10a**	NaOMe/MeOH	**12a**	50%
5	**10b**	NaOMe/MeOH	**12b**	47%
6	**10c**	NaOMe/MeOH	**12c**	45%

EXPERIMENTAL

General methods. Solutions were concentrated using an evaporator at 15–20 torr. Flash column chromatographies were carried out on silica gel (230–400 mesh). Melting points were determined on a hot stage and are uncorrected. Optical rotations were measured on a Propol Polarimeter, Model Dr. Kerchen. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker AC-250-WB or AM-400-WB instruments at 250 or 400 MHz and 62.5 or 100 MHz for ^{1}H and ^{13}C, respectively. Infrared spectra were recorded on a Nicolet 5 ZDX spectrophotometer. Electron impact mass spectra were performed on a Hewlett-Packard 5985B instrument at 70 eV. Microanalyses were performed at the Servei d'Anàlisi Química de la Universitat Autònoma de Barcelona.

(1*S*,2*R*,5*R*,6*S*,7*R*)-5-Pivaloyloxymethyl-4-oxatricyclo[5.2.1.0^{2,6}]dec-8-en-3-one (5) and (1*R*,2*R*,5*R*,6*S*,7*S*)-5-Pivaloyloxymethyl-4-oxatricyclo[5.2.1.0^{2,6}]dec-8-en-3-one (6). A mixture of (-)-(*S*)-5-pivaloyloximethyl-2(5*H*)-furanone **4a** (1.60 g, 8.1 mmol), freshly distilled cyclopentadiene (16 mL) and hydroquinone was introduced into a glass reactor fitted with a Teflon stopper and heated at 110°C for 19 h. The reaction mixture was cooled, diluted with CH_2Cl_2 and filtered to remove polymeric materials. The solvent and the excess of diene were evaporated under reduced pressure, and the resulting residue was purified by chromatography (3:1 hexane-ether). The first fraction gave **5** (1.32 g, 5.0 mmol, 62%) as a white solid: mp 80–82°C (hexane-ether); $[\alpha]_D$ − 37.6 (*c* 1.01, $CHCl_3$); IR (KBr) ν 2973, 1750 ($\nu_{C=O}$), 1729 ($\nu_{C=O}$), 1272 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.19 (s, 9H, (C(C*H*$_3$)$_3$), 1.43 (d, J_{gem} = 8.8 Hz, 1H, H-10a), 1.63 (dt, J_{gem} = 8.8 Hz, $J_{10b,1} \approx J_{10b,7}$ = 1.6 Hz, 1H, H-10b), 2.83 (ddd, $J_{6,2}$ = 9.0 Hz, $J_{6,7}$ = 4.0 Hz, $J_{6,5}$ = 2.9 Hz, 1H, H-6), 3.10 (ddd, $J_{7,6}$ = 4.0 Hz, $J_{7,8}$ = 2.9 Hz, $J_{7,10b}$ = 1.6 Hz, 1H, H-7), 3.25 (dd, $J_{2,6}$ = 9.0 Hz, $J_{2,1}$ = 4.5 Hz, 1H, H-2), 3.31 (ddd, $J_{1,2}$ = 4.5 Hz, $J_{1,9}$ = 2.9 Hz, $J_{1,10b}$ = 1.6 Hz, 1H, H-1), 4.10 (m, 2H, H-11a, H-11b), 4.19 (m, 1H, H-5), 6.24 (dd, $J_{8,9}$ = 5.6 Hz, $J_{8,7}$ = 2.9 Hz, 1H, H-8), 6.29 (dd, $J_{9,8}$ = 5.8 Hz, $J_{9,1}$ = 2.9 Hz, 1H, H-9); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 27.1 (C(*C*H$_3$)$_3$), 38.8 (*C*(CH$_3$)$_3$), 43.2 (C-6), 45.6 (C-1), 45.8 (C-7), 48.3 (C-2), 51.7 (C-10), 65.7 (C-11), 79.3 (C-5), 134.3 (C-8), 136.9 (C-9), 177.1 (C=O), 178.0 (C=O); MS (EI) *m/z* (%) 265 (M$^+$, 3), 199 (9), 149 (9), 97 (48), 93 (1), 66 (100), 41 (16).

Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16, H, 7.63. Found: C, 68.25; H, 7.36.

The second fraction gave **6** (0.40 g, 1.5 mmol, 19%) as a colorless oil; $[\alpha]_D$ + 57.7 (*c* 1.29, $CHCl_3$); IR (film) ν 2981, 1771 ($\nu_{C=O}$), 1736 ($\nu_{C=O}$), 1286 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.17 (s, 9H, (C(C*H*$_3$)$_3$), 1.48 (d, J_{gem} = 9.6 Hz, 1H, H-10a), 1.53 (dt, J_{gem} = 9.6 Hz, $J_{10b,1} \approx J_{10b,7}$ = 1.3 Hz, 1H, H-10b), 2.26 (dd, $J_{6,2}$ = 8.3 Hz, $J_{6,5}$ = 3.5 Hz, 1H, H-6), 2.65 (d, $J_{2,6}$ = 8.3 Hz, 1H, H-2), 2.91 (dt, $J_{7,8}$ = 3.0 Hz, $J_{7,1} \approx J_{7,10b}$ = 1.3 Hz, 1H, H-7), 3.25 (dd, $J_{1,9}$ = 3.0, $J_{1,10b}$ = 1.3 Hz, 1H, H-1), 4.12 (dd, J_{gem} = 12.1 Hz, $J_{11b,5}$ = 4.0 Hz, 1H, H-11b), 4.24 (dd, J_{gem} = 12.1 Hz, $J_{11a,5}$ = 3.2 Hz, 1H, H-11a), 4.33 (ddd, $J_{5,11b}$ = 4.0 Hz, $J_{5,6}$ = 3.5 Hz, $J_{5,11a}$ = 3.2 Hz, 1H, H-5), 6.16 (dd, $J_{8,9}$ = 5.6 Hz, $J_{8,7}$ = 3.0 Hz, 1H, H-8), 6.22 (dd, $J_{9,8}$ = 5.6 Hz, $J_{9,1}$ = 3.0 Hz, 1H, H-9); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 27.0 (C(*C*H$_3$)$_3$), 38.7 (*C*(CH$_3$)$_3$), 43.3 (C-10), 44.7, 46.4, 47.5 (C-1, C-6, C-7), 48.6 (C-2), 65.5 (C-11), 80.5 (C-5), 137.5 (2C, C-8,C-9), 176.6 (C=O), 177.8 (C=O); MS (EI) *m/z* (%) 264 (M$^+$, 1), 97 (47), 85 (6), 57 (23).

Anal. Calcd. for ($C_{15}H_{20}O_4$): C, 68.16; H, 7.63. Found: C, 67.97; H, 7.62.

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(1*S*,2*R*,5*R*,6*S*,7*R*)-2-Methyl-5-pivaloyloxymethyl-4-oxatricyclo[5.2.1.0^{2,6}]dec-8-en-3-one (7) and (1*R*,2*R*,5*R*,6*S*,7*S*)-2-Methyl-5-pivaloyloxymethyl-4-oxatricyclo[5.2.1.0^{2,6}]dec-8-en-3-one (8). *n*-BuLi (1.6 M in hexane, 2.33 mL, 3.78 mmol) was added to a stirred solution of freshly distilled diisopropylamine (0.53 mL, 3.78 mmol) in dry THF (30 mL) at −78°C under Ar atmosphere. After 20 min, a solution of a mixture of the *endo*/*exo* cycloadducts **5** and **6** (500 mg, 1.89 mmol) in THF (7 mL) was added dropwise. The mixture was kept at −78°C for 1 h. Then, methyl iodide (10.5 mL, 0.16 mmol) was added. After 2 h at −78°C, the solution was allowed to warm to rt, diluted with CH_2Cl_2, washed with 1% aq HCl solution and dried (Na_2SO_4). The solvents were evaporated and the residue was chromatographed (5:1 hexane-EtOAc) to afford a mixture of **7** and **8** (420 mg, 1.51 mmol, 80%). A second column chromatography (10:1 hexane-EtOAc) allowed the separation of pure **7** and **8**. **7**: white solid: mp 145–147°C (hexane-EtOAc); $[\alpha]_D$ + 13.9 (*c* 3.30, $CHCl_3$); IR (KBr) ν 2973, 1764 ($\nu_{C=O}$), 1729 ($\nu_{C=O}$), 1286, 1223, cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20 (s, 9H, C(C*H*$_3$)$_3$), 1.51 (s, 3H, Me), 1.66 (m, 2H, H-10a, H-10b), 2.38 (dd, $J_{6,7}$ = 4.0 Hz, $J_{6,5}$ = 3.0 Hz, 1H, H-6), 2.82 (m, 1H, H-1), 3.04 (m, 1H, H-7), 4.08 (m, 2H, H-5, H-11a), 4.14 (dd, J_{gem} = 13.9 Hz, $J_{11b,5}$ = 5.9 Hz, 1H, H-11b), 6.23 (dd, $J_{8,9}$ = 5.6 Hz, $J_{8,7}$ = 2.9 Hz, 1H, H-8), 6.30 (dd, $J_{9,8}$ = 5.6 Hz, $J_{9,1}$ = 3.0 Hz, 1H, H-9); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 23.4 (CH_3), 27.1 (C(*C*H$_3$)$_3$), 38.8 (*C*(CH$_3$)$_3$), 46.4 (C-7), 49.5 (C-10), 50.4 (C-6), 51.9 (C-1), 54.3 (C-2), 66.0 (C-11), 78.1 (C-5), 134.5 (C-8), 137.9 (C-9), 178.2 (C=O), 180.1 (C=O); MS (EI) *m*/*z* (%) 185 (7), 140 (6), 111 (100), 98 (34), 86 (93), 69 (31), 66 (7), 41 (57).

Anal. Calcd for ($C_{16}H_{22}O_4$): C, 69.04; H, 7.97. Found: C, 68.96; H, 7.84.

8: oil; $[\alpha]_D$ + 0.82 (*c* 2.45, $CHCl_3$); IR (film) ν 2981, 1764 ($\nu_{C=O}$), 1729 ($\nu_{C=O}$), 1286, 1152 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20 (s, 9H, C(C*H*$_3$)$_3$), 1.24 (s, 3H, Me), 1.54 (m, 2H, H-10a, H-10b), 1.72 (m, 1H, H-6), 2.88 (m, 1H, H-1), 2.92 (m, 1H, H-7), 4.07 (dd, J_{gem} = 12.2 Hz, $J_{11a,5}$ = 5.5 Hz, 1H, H-11a), 4.21 (dd, J_{gem} = 12.2 Hz, $J_{11b,5}$ = 5.5 Hz, 1H, H-11b), 4.29 (ddd, $J_{5,11b}$ = 5.5 Hz, $J_{5,11a}$ = 4.3 Hz, $J_{5,6}$ = 3.1 Hz, 1H, H-5), 6.20 (dd, $J_{8,9}$ = 5.5 Hz, $J_{8,7}$ = 3.1 Hz, 1H, H-8), 6.27 (dd, $J_{9,8}$ = 5.5 Hz, $J_{9,1}$ = 3.1 Hz, 1H, H-9); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 21.7 (CH_3), 27.1 (C(*C*H$_3$)$_3$), 38.8 (*C*(CH$_3$)$_3$), 45.4 (C-7), 49.3 (C-10), 50.3 (C-6), 50.6 (C-1), 54.2 (C-2), 65.9 (C-11), 80.0 (C-5), 136.4 (C-8), 137.0 (C-9), 178.2 (C=O), 180.7 (C=O); MS (EI) *m*/*z* (%) 111 (92), 98 (41), 86 (100), 83 (50), 65 (8), 57 (2), 55 (39), 41 (41).

Anal. Calcd for ($C_{16}H_{22}O_4$): C, 69.04; H, 7.97. Found: C, 69.00; H, 7.79.

(*S*)-3-Methyl-5-pivaloyloxymethyl-2(5*H*)-furanone (4c). A solution of **7** and **8** (294 mg, 1.06 mmol) in benzene (20 mL) was heated for 8 days in a sealed tube. Evaporation of the solvent and chromatography (1:1 hexane-ether) afforded **4c** (160 mg, 0.75 mmol, 71%) as a colorless oil. $[\alpha]_D$ − 63.2 (*c* 0.75, $CHCl_3$); IR (film) ν 2973, 1757 ($\nu_{C=O}$), 1722 ($\nu_{C=O}$), 1279, 1173 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.18 (s, 9H, C(C*H*$_3$)$_3$), 1.90 (m, 3H, CH_3), 4.27 (d, 2H, H-6a, H-6b), 5.40 (m, 1H, H-5), 6.95 (m, 1H, H-4); ^{13}C RMN (62.5 MHz, $CDCl_3$) δ 10.5 (*C*H$_3$), 26.9 (C(*C*H$_3$)$_3$), 38.7 (*C*(CH$_3$)$_3$), 62.3 (C-6), 78.8 (C-5), 131.7 (C-3), 144.5 (C-4), 173.4 (C=O), 177.8 (C=O); MS (EI) *m*/*z* (%) 213 (M^+ + 1, 6), 154 (4), 156 (1), 112 (26), 111 (43), 98 (43), 85 (31), 69 (12), 57 (100), 41 (46).

Anal. Calcd for ($C_{11}H_{16}O_4$): C, 62.25; H, 7.60. Found: C, 61.99; H, 7.50.

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(1*S*,4*S*,5*S*,6*S*,7*R*)-6,7-Carbonyldioxy-1-methyl-4-pivaloyloxymethyl-3-oxabicyclo[3.2.0]heptan-2-one (10c). A solution of **4c** (160 mg, 0.75 mmol) and vinylene carbonate (0.23 mL, 3.62 mmol) in freshly distilled acetone (65 mL) was irradiated in a small conventional photochemical reactor (two-necked vessel fitted with a Pyrex immersion-type cooling jacket) using a medium-pressure 125W mercury lamp at −78°C for 8 h under Ar atmosphere. Evaporation of the solvent and chromatography of the residue (from 0 to 15% of EtOAc in hexane) afforded the recovered lactone **4c** (5 mg, 0.02 mmol, 3%), and then the cycloadduct **10c** (137 mg, 0.46 mmol, 61%) as a white solid: mp 155–157°C (hexane-EtOAc); $[\alpha]_D$ − 31.7 (*c* 0.81, $CHCl_3$); IR (KBr) ν 3466, 2981, 1799 ($\nu_{C=O}$), 1771 ($\nu_{C=O}$), 1736 ($\nu_{C=O}$), 1286, 1145 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.19 (s, 9H, $C(CH_3)_3$), 1.54 (s, 3H, CH_3), 2.89 (dd, $J_{5,6}$ = 1.8 Hz, $J_{5,4}$ = 1.5 Hz, 1H, H-5), 4.18 (dd, J_{gem} = 12.3 Hz, $J_{8b,4}$ = 4.4 Hz, 1H, H-8b), 4.23 (dd, J_{gem} = 12.3 Hz, $J_{8a,4}$ = 4.1 Hz, 1H, H-8a), 4.78 (ddd, $J_{4,8b}$ = 4.4 Hz, $J_{4,8a}$ = 4.1 Hz, $J_{4,5}$ = 1.5 Hz, 1H, H-4), 4.99 (dd, $J_{6,7}$ = 5.6 Hz, $J_{6,5}$ = 1.8 Hz, 1H, H-6), 5.04 (d, $J_{7,6}$ = 5.6 Hz, 1H, H-7); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 14.3 (CH_3), 27.1, ($C(CH_3)_3$), 38.9 ($C(CH_3)_3$), 49.1 (C-5), 50.3 (C-1), 64.6 (C-8), 77.0, 77.7, 78.0 (C-4, C-6, C-7), 154.1 (C=O), 175.6 (C=O), 177.9 (C=O); MS (CI, NH_3) *m*/*z* 316 (M^++ 18, 100), 299 (2), 272 (1).

Anal. Calcd for ($C_{14}H_{18}O_7$): C, 56.37; H, 6.08. Found: C, 56.54; H: 5.85.

5-*O*-Pivaloyl-3-*C*-(carboxymethyl)-3-deoxy-2,3-γ-lactone-α-D-lyxofuranose (12a). Compound **10a** (300 mg, 1.06 mmol) was dissolved in a solution of NaOH in aq dioxane 50% (3 mL, 0.5 M). The mixture was stirred at rt for 30 min. The solution was neutralized with 5% aq HCl, and the resulting mixture was extracted with CH_2Cl_2 (3 × 5 mL) and EtOAc (3 × 5 mL). The organic layers were combined, washed with brine and dried (Na_2SO_4). Evaporation of the solvent and crystallization from pentane-EtOAc afforded **12a** (96 mg, 0.34 mmol, 33%) as a white solid: mp 122–124°C; $[\alpha]_D$ + 41.8 (*c* 1.01, $CHCl_3$); IR (KBr) ν 3381, 2973, 1778 ($\nu_{C=O}$), 1729 ($\nu_{C=O}$), 1181 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.21 (s, 9H, $C(CH_3)_3$), 2.60 (m, 2H, H-1′a, H-1′b), 2.85 (d, $J_{OH,1}$ = 1.8 Hz, 1H, OH), 3.25 (dq, $J_{3,2}$ = 6.9 Hz, $J_{3,1'a} \approx J_{3,1'b} \approx J_{3,4}$ = 5.9 Hz, 1H, H-3), 4.20 (dd, J_{gem} = 12.1 Hz, $J_{5a,4}$ = 5.9 Hz, 1H, H-5a), 4.29 (dd, J_{gem} = 12.1 Hz, $J_{5b,4}$ = 5.9 Hz, 1H, H-5b), 4.55 (q, $J_{4,5a} \approx J_{4,5b} \approx J_{4,3}$ = 5.9 Hz, 1H, H-4), 4.91 (d, $J_{2,3}$ = 6.9 Hz, 1H, H-2), 5.51 (d, $J_{1,OH}$ = 1.8 Hz, 1H, H-1); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 27.0 ($C(CH_3)_3$), 28.1 (C-1′), 29.7 ($C(CH_3)_3$), 38.7 (C-3), 62.1 (C-5), 76.2 (C-4), 87.1 (C-2), 100.2 (C-1), 175.6 (C=O), 178.1 (C=O); MS (CI/NH_3) *m*/*z* (%) 276 (M^+ + 18, 100), 274 (3), 260 (1), 259 (5), 241 (2).

Anal. Calcd for ($C_{12}H_{18}O_6$): C, 55.81; H, 7.02. Found: C, 56.00; H, 6.78.

When the cycloadduct **10a** (90 mg, 0.32 mmol) was treated with NaOMe (3 mg, 0.05 mmol) in dry MeOH (10 mL) under Ar atmosphere for 3 h at rt, compound **12a** was obtained (40 mg, 0.16 mmol, 50%) after the usual work-up and purification by column chromatography (5:1 hexane-EtOAc).

5-*O*-Pivaloyl-3-*C*-(carboxymethyl)-3-deoxy-3-methyl-2,3-γ-lactone-α-D-lyxofuranose (12b). Cycloadduct **10b** (400 mg, 1.34 mmol) was dissolved in a solution of NaOH in aq dioxane 50% (2.4 mL, 0.5 M). The mixture was stirred at rt for 30 min. The solution was neutralized with 5% aq HCl, and the resulting mixture was extracted with CH_2Cl_2 (3 × 5 mL) and EtOAc (3 × 5 mL). The organic layers were combined,

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washed with brine and dried (Na_2SO_4). Evaporation of the solvent and crystallization from pentane-EtOAc afforded **12b** (120 mg, 0.44 mmol, 33%) as a white solid: mp 95–97°C; $[\alpha]_D$ + 44.6 (*c* 0.61, acetone); IR (KBr) ν 3402, 2987, 1778 ($\nu_{C=O}$), 1743 ($\nu_{C=O}$), 1356, 1286 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.19 (s, 9H, $C(CH_3)_3$), 1.45 (s, 3H, CH_3), 2.29 (d, J_{gem} = 18.3 Hz, 1H, H-1′a), 2.74 (d, J_{gem} = 18.3 Hz, 1H, H-1′b), 3.35 (d, $J_{OH,1}$ = 2.2 Hz, 1H, OH), 4.20 (m, 3H, H-5a, H-5b, H-4), 4.45 (s, 1H, H-2), 5.41 (d, $J_{1,OH}$ = 2.2 Hz, 1H, H-1); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 23.8 (CH_3), 27.0 ($C(CH_3)_3$), 35.6 (C-1′), 38.7 ($C(CH_3)_3$), 47.3 (C-3), 62.3 (C-5), 81.6 (C-4), 93.3 (C-2), 100.0 (C-1), 175.2 (C=O), 178.1 (C=O); MS (CI/NH_3) *m/z* (%) 290 (M^+ + 18, 100), 289 (2), 288 (10), 273 (1).

Anal. Calcd for ($C_{13}H_{20}O_6$): C, 57.34; H, 7.40. Found: C, 57.36; H, 7.23.

When the cycloadduct **10b** (100 mg, 0.37 mmol) was treated with NaOMe (3 mg, 0.05 mmol) in dry MeOH (10 mL) under Ar atmosphere for 3 h at rt, compound **12b** was obtained (44 mg, 0.16 mmol, 47%) after the usual work-up and purification by column chromatography (4:1 hexane-EtOAc).

5-*O*-Pivaloyl-3-*C*-(carboxymethylmethyl)-3-deoxy-2,3-γ-lactone-α-D-lyxofuranose (12c). Cycloadduct **10c** (400 mg, 1.34 mmol) was dissolved in a solution of NaOH in aq dioxane 50% (2.4 mL, 0.5 M). The mixture was stirred at rt for 30 min. The solution was neutralized with 5% aq HCl, and the resulting mixture was extracted with CH_2Cl_2 (3 × 5 mL) and EtOAc (3 × 5 mL). The organic layers were combined, washed with brine and dried (Na_2SO_4). Evaporation of the solvent and chromatography (4:1 hexane-EtOAc) afforded **12c** (113 mg, 0.42 mmol, 31%) as an oil. $[\alpha]_D$ + 38.7 (*c* 0.82, $CHCl_3$); IR (film) ν 3444, 2980, 1778 ($\nu_{C=O}$), 1729 ($\nu_{C=O}$), 1286, 1159 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.19 (s, 9H, $C(CH_3)_3$), 1.32 (d, $J_{Me,1'}$ = 7.4 Hz, 3H, Me), 2.68 (dq, $J_{1',Me}$ = 7.4 Hz, $J_{1',3}$ = 4.4 Hz, 1H, H-1′), 2.74 (br, 1H, OH), 2.86 (ddd, $J_{3,2}$ = 7.4 Hz, $J_{3,4}$ = 5.6 Hz, $J_{3,1'}$ = 4.4 Hz, 1H, H-3), 4.22 (dd, J_{gem} = 11.9 Hz, $J_{5a,4}$ = 6.2 Hz, 1H, H-5a), 4.28 (dd, J_{gem} = 11.9 Hz, $J_{5b,4}$ = 5.9 Hz, 1H, H-5b), 4.55 (ddd, $J_{4,5a}$ = 6.2 Hz, $J_{4,5b}$ = 5.9 Hz, $J_{4,3}$ = 5.6 Hz, 1H, H-4), 4.86 (d, $J_{2,3}$ = 7.4 Hz, 1H, H-2), 5.50 (s, 1H, H-1); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 16.9 (CH_3), 27.0 ($C(CH_3)_3$), 33.9 (C-1′), 38.7 ($C(CH_3)_3$), 47.8 (C-3), 62.0 (C-5), 76.1 (C-4), 85.6 (C-2), 100.5 (C-1), 178.0 (C=O), 178.6 (C=O); MS (CI/NH_3) *m/z* (%) 290 (M^++ 18, 100), 288 (14), 279 (14), 255 (10), 248 (67), 204 (7).

Anal. Calcd for ($C_{13}H_{20}O_6$): C, 57.34; H, 7.40. Found: C, 57.30; H, 7.23.

When the cycloadduct **10c** (110 mg, 0.37 mmol) was treated with NaOMe (3 mg, 0.05 mmol) in dry MeOH (10 mL) under Ar atmosphere for 3 h at rt, compound **12c** was obtained (45 mg, 0.16 mmol, 45%) after the usual work-up and purification by column chromatography (4:1 hexane-EtOAc).

(1*R*,4*S*,5*R*,6*R*,7*S*)-6,7-Dihydroxy-5-methyl-4-pivaloyloxymethyl-3-oxabicyclo[3.2.0]heptan-2-one (13b). Compound **11b** (70 mg, 0.23 mmol) was dissolved in a solution of NaOH in aq dioxane 50% (1.0 mL, 0.5 M). The mixture was stirred at rt for 4 h. The solution was neutralized with 5% aq HCl, and the resulting mixture was extracted with CH_2Cl_2 (3 × 5 mL) and EtOAc (3 × 5 mL). The organic layers were combined, washed with brine and dried (Na_2SO_4). Evaporation of the solvent and column chromatography (3:1 hexane-EtOAc) afforded **13b** (26 mg, 0.09 mmol, 41%) as a white solid: mp 105–107°C (hexane-EtOAc); IR (KBr) ν 3459, 2966, 2924, 1729

($\nu_{C=O}$), 1152, 1124 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.18 (s, 9H, $C(CH_3)_3$), 1.39 (s, 3H, CH_3), 2.74 (d, $J_{1,7}$ = 1.2 Hz, 1H, H-1), 3.16 (br, 1H, OH), 3.27 (br, 1H, OH), 4.32 (m, 3H, H-8a, H-8b, H-4), 4.39 (d, $J_{6,7}$ = 5.5 Hz, 1H, H-6), 4.49 (dd, $J_{7,6}$ = 5.5 Hz, $J_{7,1}$ = 1.2 Hz, 1H, H-7); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 15.4 (CH_3, C-13), 27.0 ($C(CH_3)_3$), 38.8 ($C(CH_3)_3$), 49.6 (C-1), 61.7 (C-8), 66.4 (C-7), 72.0 (C-6), 83.7 (C-4), 175.3 (C=O), 178.5 (C=O); MS (CI/NH_3) *m/z* (%) 290 (M^+ + 18, 100), 291 (15), 292 (2), 288 (1), 276 (2).

Anal. Calcd for ($C_{13}H_{20}O_6$): C, 57.34; H, 7.40. Found: C, 57.31; H, 7.28.

When the cycloadduct **11b** (60 mg, 0.20 mmol) was treated with NaOMe (3 mg, 0.05 mmol) in dry MeOH (10 mL) under Ar atmosphere for 3 h at rt, compound **13b** was obtained (25 mg, 0.09 mmol, 45%) after the usual work-up and purification by column chromatography (4:1 hexane-EtOAc).

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