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Cobalt-Catalyzed Diastereoselective Synthesis of *C*-Furanosides. Total Synthesis of (−)-Isoaltholactone

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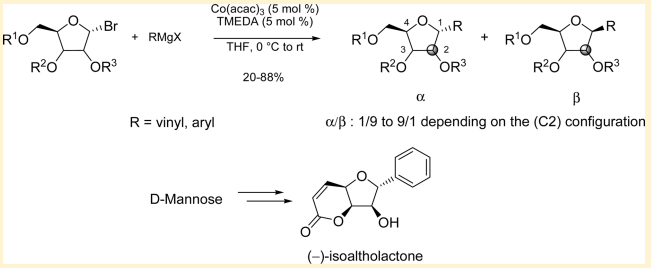
Supporting Information

ABSTRACT: An array of *C*-aryl and *C*-vinyl furanosides were prepared in good yields and diastereoselectivities from *C*-halogeno furanosides either with aryl Grignard or with vinyl Grignard using the convenient $Co(acac)_3$/TMEDA catalytic system. This method is illustrated by the total synthesis of the (−)-isoaltholactone.



INTRODUCTION

C-Glycosides and *C*-furanosides are a rich source of building blocks to access biologically active cyclic ethers and are potent targets for the pharmaceutical industry.[1,2] In addition, non-natural *C*-aryl furanosides, as nucleoside derivatives, provide research opportunities for the study and probing of nucleobases.[3,4]

C-glycosides can be prepared according to different methods;[5,6] however, the formation of the anomeric C−C bond by a metal-catalyzed cross-coupling between *C*-halogeno glycosides and organometallics represents an attractive method. For instance, Lemaire et al. have reported that the addition of stoichiometric amounts of Ar_2Zn reagents to 1-bromo glycosides provides *C*-aryl glycosides with full *β*-selectivities in the glucose series and *α*-selectivities in the mannose series.[7] In addition, to form the *C*-aryl and *C*-alkyl bonds, Gagné et al. described a diastereoselective Negishi coupling catalyzed by $Ni(COD)_2$/*t*Bu-Terpy yielding glycosides with *β*-selectivities in the glucose and galactose series, and *α*-selectivities in the mannose series.[8] Among the different approaches,[9] the metal-catalyzed cross-coupling between *C*-halogeno furanosides and organometallics represents a powerful tool for the preparation of *C*-aryl furanosides.[10−14] Therefore, the development of a simple and unified method for the synthesis of *C*-glycosides and *C*-furanosides would represent a major breakthrough in the field of carbohydrate chemistry. As part of our efforts for the synthesis of natural products from carbohydrate-based building blocks[15] and nonexpensive metal-catalyzed reactions,[16] we recently described the synthesis of *C*-aryl and *C*-vinyl glycosides using a diastereoselective cobalt-catalyzed cross-coupling between *C*-bromo glycosides and Grignard reagents.[17] The *C*-aryl and *C*-vinyl glycosides were obtained with good *α*-selectivities and, in addition, we have demonstrated that a radical process was operating in the mechanism of the cross-coupling.[17]

Herein, we wish to report the synthesis of substituted *C*-furanosides by cobalt-catalyzed cross-coupling of *C*-bromo furanosides with Grignard reagents, and the application of this method to the synthesis of the enantiomer of the antitumor natural product (+)-isoaltholactone.

RESULTS AND DISCUSSION

Preparation of Substituted *C*-Aryl and *C*-Vinyl Furanosides. As an extension of the *C*-aryl and *C*-vinyl glycosides, an array of orthogonally protected *C*-halogeno furanosides **1**−**7**[18] was prepared and these compounds were subjected to the cobalt-catalyzed cross-coupling with phenylmagnesium bromide to prepare the corresponding *C*-phenyl furanosides (Table 1). When 1-bromo furanosides **1**[19] was treated with PhMgBr (1.5 equiv) in the presence of $Co(acac)_3$ (5 mol %) and TMEDA (5 mol %) (Table 1, entry 1), the 1,4-*cis* furan was obtained in low yield (22%), due to the high instability of the starting material. The *tert*-butyldiphenylsilyl protected or benzoyl protected *C*-bromo furanosides **2** and **3** yielded the 1,4-*cis* furans in 77% and 76% yield, respectively, and the corresponding *trans*-diastereoisomers were not isolated (Table 1, entries 2 and 3). However, when the configuration of the C2/C3 stereocenters was inverted such as in *C*-bromo furanosides **4**, **5**, and **6**,[20] the 1,4-*trans* *C*-phenyl furans were isolated in 62%, 88%, and 75% yields, respectively (Table 1, entries 4, 5, and 6). In the absence of any substituent at C2,

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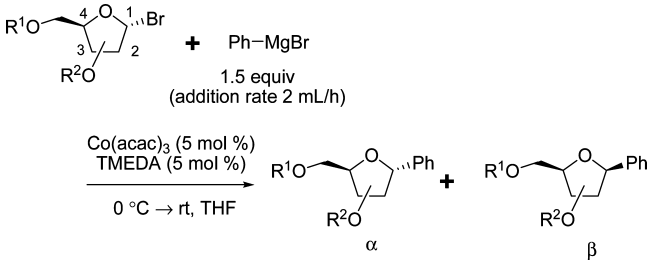
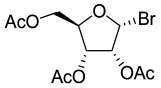
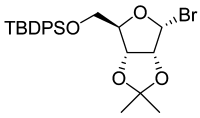
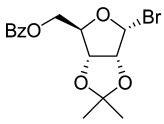
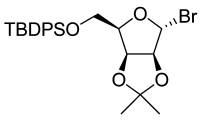
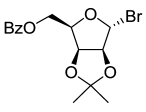
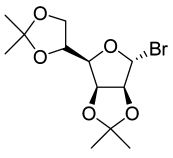
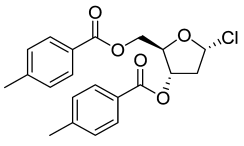
Table 1. Scope of the Cobalt-Catalyzed Cross-Coupling *C*-Halogeno Furanosides 1-7 with PhMgBr[a]



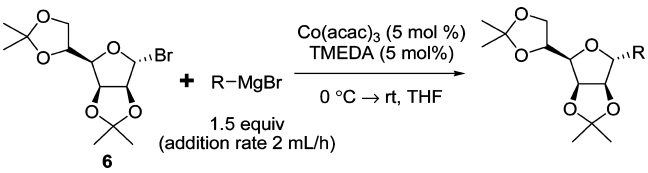
entry	reagent	dr (α/β) [b]	yield (%) [c]
1	 **1**	> 1:9	22
2	 **2**	> 1:9	77
3	 **3**	> 1:9	76
4	 **4**	> 9:1	62
5	 **5**	> 9:1	88
6	 **6**	> 9:1	75
7	 **7**	1.3:1	60

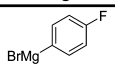
[a]PhMgBr (1.5 equiv) was added at a rate of 2 mL/h; once the reaction was complete the reaction medium was warmed to rt. [b]Determined by ^{1}H NMR spectroscopy. [c]Yield of isolated product.

almost no selectivity was observed for the cross-coupling product. Indeed, the cross-coupling between Hoeffer's chlororibofuranose **7**[21] and phenylmagnesium bromide afforded the desired compound in 60% yield with poor diastereoselectivity (α/β = 1.3:1) (Table 1, entry 7). Therefore, contrary to the *C*-bromo glycosides, the diastereoselectivity of the cobalt-catalyzed cross-coupling of *C*-halogeno furanosides is controlled by the substituent present at C2.

A range of Grignard reagents was examined using **6** as the *C*-bromo furanoside. 4-Fluorophenylmagnesium bromide reacted with **6** to produce the coupling product in a good yield of 97% and a α/β diastereoselectivity superior to 9:1 (Table 2, entry 1). When 2-thienylmagnesium bromide was employed, a 53% yield was obtained for the coupling product, even with an increase of the catalytic charge [Co(acac)$_3$ (10 mol %)/TMEDA (15 mol %)] (Table 2, entry 2). The cross-coupling was also operative with 2-methyl-1-propenylmagnesium bromide and the corresponding *C*-vinyl furanoside was isolated in 66% and with a α/β diastereoselectivity superior to 9:1 (Table 2, entry 3).

Table 2. Scope of the Cobalt-Catalyzed Cross-Coupling of Grignard Reagents and *C*-Bromo Furanoside 6[a]

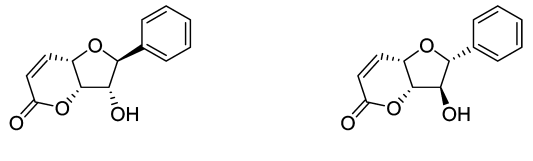


entry	R-MgBr	dr (α/β) [b]	yield (%) [c]
1		> 9:1	97
2		> 9:1	53 [d]
3		> 9:1	66

[a]Grignard reagent (1.5 equiv) was added at a rate of 2 mL/h; once the reaction was complete the reaction medium was warmed to rt. [b]Determined by ^{1}H NMR spectroscopy. [c]Yield of isolated product. [d]Co(acac)$_3$ (10 mol %) and TMEDA (15 mol %) were used.

Total Synthesis of (−)-Isoaltholactone. To illustrate the potential of the cobalt-catalyzed cross-coupling of aryl Grignard reagents with *C*-halogeno furanosides, the synthesis of (−)-isoaltholactone was envisaged from the natural D-mannose and designed to prove that our method can be included in multistep synthesis.

(+)-Isoaltholactone (+)-**8** (Figure 1), a diastereoisomer of the antitumor agent (+)-altholactone (+)-**9**,[22] was originally isolated from combined extracts of *Goniuothalamus malayanus*, *G. montanus*, and *G. tapis*.[23] This lactone exhibits significant biological activities including antitumoral, antifungal, and antibacterial activities.[27,24] The growing interest among the scientific community for this natural product also led to the synthesis of different analogues of **8**.[25] The early approaches



(+)-Isoaltholactone, (+)-**8** (+)-Altholactone, (+)-**9**

Figure 1. Structures of (+)-isoaltholactone, (+)-**8**, and (+)-altholactone, (+)-**9**.

include an epoxidation followed by a cyclization in order to install the C2- and C3-stereogenic centers,[29,26] and an asymmetric Pd-catalyzed cross-coupling to introduce the phenyl group.[29,27] Direct syntheses from natural-based building blocks were also realized.[28] To our knowledge, the preparation of **8** by a metal-catalyzed cross-coupling from a *C*-halogeno furanoside has never been realized.

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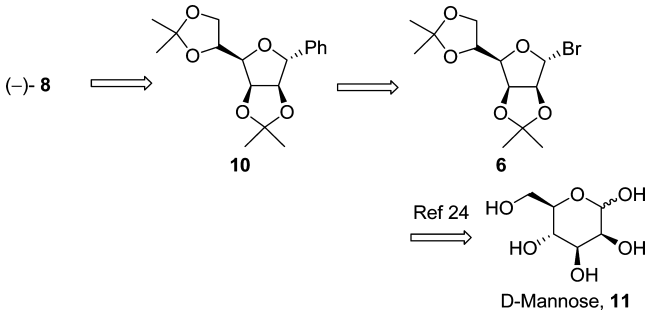
In our retrosynthetic analysis (Scheme 1), the *Z* double bond of (−)-isoaltholactone **8** would be introduced by a Still-Gennari reaction applied to an aldehyde coming from the selective cleavage of the acetonide at C4 of *C*-furanoside **10**, followed by an oxidative cleavage of the obtained diol. *C*-Furanoside **10** would be prepared through the cobalt-catalyzed cross-coupling between *C*-bromo furanoside **6** and phenylmagnesium bromide (Table 1, entry 6), and **6** would be easily synthesized in two steps from D-mannose **11** as described in the literature.[24]

Scheme 1. Retrosynthesis Analysis of (−)-Isoaltholactone (−)-8



The substituted furanoside **10** (Table 1, entry 6) was treated with 5 mol % of $BiCl_3$ in MeCN to deliver chemoselectively diol **12** in 55% yield (Scheme 2). Oxidative cleavage of this 1,2-diol with $NaIO_4$ (THF/pH 7 buffer) afforded the corresponding aldehyde **13**, which was directly treated with the Still-Gennari phosphonoacetate **I**, providing α,β-unsaturated ester **14** in 51% yield (two steps). Finally, a one-pot acetonide deprotection/transesterification sequence using a catalytic amount of *p*-toluenesulfonic acid provided (−)-**8** in quantitative yield. (−)-Isoaltholactone **8** was prepared in 7 steps from D-mannose in 20% global yield. The optical rotation ($[\alpha]_D^{20}$ −23.0 (*c* = 0.15, EtOH);[28b] natural product: $[\alpha]_D^{20}$ + 20.0 (*c*= 0.20, EtOH)[26f]) and the spectroscopic data of (−)-**8** were in agreement with those reported in the literature.[26f,28b]

CONCLUSION

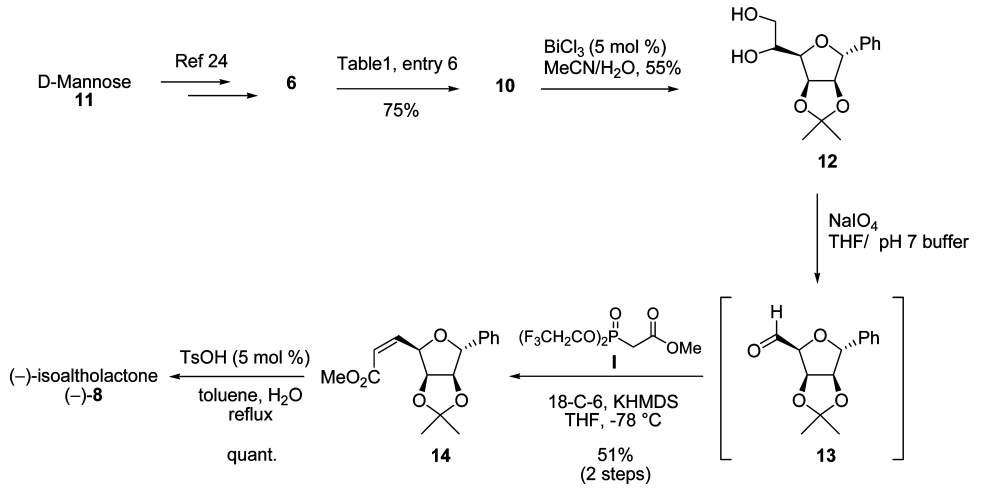
In summary, we have developed a diastereoselective cobalt-calatyzed cross-coupling of *C*-halogeno furanosides with aryl and vinyl Grignard reagents using a cheap and convenient $Co(acac)_3$/TMEDA catalytic system, providing *C*-furanosides in moderate to good yields. Contrary to the *C*-bromo-glycosides,[17] the orthogonally protected *C*-halogeno furanosides displayed a different behavior as the obtained selectivities were dependent on the C2 substituent. This cross-coupling was finally utilized to access (−)-isoaltholactone in seven steps and in 20% overall yield for D-mannose.

EXPERIMENTAL SECTION

General Experimental Methods. ^1H NMR spectra were recorded at 400 MHz and data are reported as follows: chemical shift in ppm from tetramethylsilane as an internal standard with the residual solvent peak as an internal indicator ($CDCl_3$ δ: 7.26, C_6D_6 δ: 7.16), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet or overlap of nonequivalent resonances, br = broad), integration. ^{13}C NMR spectra were recorded at 100 MHz and the data are reported as follows: chemical shift in ppm from tetramethylsilane as an internal standard with the residual solvent peak as an internal indicator ($CDCl_3$ δ: 77.16, C_6D_6 δ: 128.06). THF was dried over Na/benzophenone prior to distillation or using a solvent purification system. TMEDA was dried over CaH_2 prior to distillation. TLC was performed on silica gel plates visualized either with a UV lamp (254 nm) or using solution of *p*-anisaldehyde-sulfuric acid-acetic acid in EtOH followed by heating. Purification was performed on silica gel (230−400 mesh). High-resolution mass spectra (HRMS) were performed using electrospray ionization (ESI) with Orbitrap mass analysis. Mass spectra with electronic impact (MS-EI) were recorded on a GC/MS (70 eV). *C*-Aryl and *C*-vinyl glycosides were prepared and described in reference 17a. The *C*-halogeno furanosides **1**,[24] **6**,[25] and **7**[26] were prepared according to reference reported procedures.

General Procedure for the Cobalt-Catalyzed Cross-Coupling. A solution of the alkenyl or aryl Grignard reagent in THF (1.5 equiv) was added dropwise (at a rate of 2 $mL.h^{-1}$ using a syringe pump) to a solution of alkyl halide (1 equiv, 0.1 M), $Co(acac)_3$ (5 mol %), and TMEDA (5 mol %) in THF at 0 °C. The reaction medium was warmed to room temperature and after 1 h (at this temperature); the reaction was quenched by adding an aqueous solution of 1 M HCl. After extractive workup, the crude product was purified by silica gel chromatography.

Scheme 2. Synthesis of (−)-Isoaltholactone[a]



[a]KHMDS = potassium bis(trimethylsilyl)amide, TsOH = *p*-toluenesulfonic acid, 18-C-6 = 1,4,7,10,13,16-hexaocyclooctadecane.

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(2*R*,3*R*,4*S*,5*S*)-2-(Acetoxymethyl)-5-phenyl-tetrahydrofuran-3,4-diyl diacetate. (from **1**, Table 1, entry 1) $[\alpha]_D^{20}$ −1.2 (*c* 0.6, $CHCl_3$); IR (neat): 2917, 1741, 1372, 1215, 1090, 1042, 901, 762, 699, 605 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.40−7.28 (m, 5H), 5.27 (t_{app}, *J* = 5.1 Hz, 1H), 5.09 (t_{app}, *J* = 5.9 Hz, 1H), 5.00 (d, *J* = 6.9 Hz, 1H), 4.45 (dd, *J* = 11.6, 2.8 Hz, 1H), 4.32 (m, 1H), 4.28 (dd, *J* = 11.6, 4.3 Hz, 1H), 2.10 (s, 6H), 2.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 169.8, 138.1, 128.6, 128.5, 126.0, 82.2, 79.8, 76.7, 71.6, 63.7, 20.9, 20.7; MS (EI) *m*/*z*: 216 (13), 174 (42), 173 (11), 161 (10), 158 (11), 157 (100), 133 (14), 131 (12), 128 (8), 115 (14), 107 (30), 105 (20), 103 (11), 91 (21), 86 (12), 85 (54), 79 (11), 77 (14), 69 (19); HRMS (ESI): Calcd for $C_{17}H_{20}O_7Na$ $[M+Na]^+$: 359.1101. Found: 359.1102.

(((3a*R*,4*R*,6*R*,6a*R*)-6-Bromo-2,2-dimethyl-tetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)methoxy)(*tert*-butyl)diphenylsilane (2). To a solution of (3a*R*,6*R*,6a*R*)-6-(Hydroxymethyl)-2,2-dimethyl-tetrahydrofuro[3,4-d][1,3]dioxol-4-ol[29] (1.14 g, 5.99 mmol) and imidazole (1.04 g, 16.7 mmol, 2.8 equiv) in dry DMF (3 mL), was added *tert*-butyl(chloro)diphenylsilane (1.8 g, 1.7 mL, 6.6 mmol, 1.1 equiv). After 2 h at room temperature, the reaction was quenched with water and extracted with CH_2Cl_2. The organic layer was washed with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the product was purified by silica-gel chromatography (PE/Et_2O, 90/10) to yield (3a*R*,6*R*,6a*R*)-6-((*tert*-Butyldiphenylsilyloxy)methyl)-2,2-dimethyl-tetrahydrofuro[3,4-d][1,3]dioxol-4-ol as a 69:31 mixture of α- and β-isomers (1.15 g, 2.34 mmol, 39%): IR (neat): 3423, 3071, 2933, 2858, 1427, 1210, 1104, 1069, 999, 870, 822, 740, 701, 613 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.69−7.63 (m, 4H), 7.48−7.40 (m, 6H), 5.63 (dd, *J* = 11.3, 4.0 Hz, 0.31H), 5.36 (d, *J* = 10.6 Hz, 0.69H), 4.78 (dd, *J* = 6.2, 0.8 Hz, 0.31H), 4.72 (brd, *J* = 5.9 Hz, 0.69H), 4.67 (dd, *J* = 6.2, 4.0 Hz, 0.31H), 4.61 (d, *J* = 5.9 Hz, 0.69H), 4.55 (d, *J* = 10.6 Hz, 0.69H), 4.29 (m, 0.69H), 4.15 (m, 0.31H), 3.96 (dd, *J* = 11.3 Hz, 0.31H), 3.83 (dd, *J* = 11.5, 2.7 Hz, 0.69H), 3.81 (dd, *J* = 11.2, 2.7 Hz, 0.31H), 3.83 (dd, *J* = 11.5, 2.7 Hz, 0.69H), 3.62 (dd, *J* = 11.2, 2.7 Hz, 0.31H), 1.56 (s, 0.93H), 1.48 (s, 2.07H), 1.40 (s, 0.93H), 1.32 (s, 2.07H), 1.09 (s, 4.14H), 1.06 (s, 1.86H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.9, 135.7, 134.9, 132.8, 132.5, 131.7, 131.6, 130.6, 130.4, 130.2, 130.1, 128.3, 128.2, 128.0, 127.8, 113.1, 112.3, 103.5, 98.2, 87.2, 82.1, 81.8, 81.4, 79.6, 66.2, 65.6, 27.0, 26.6, 26.3, 25.1, 24.8, 19.2; MS (EI) *m*/*z*: 413 ($[M-Me]^+$, 2), 187 (29), 257 (14), 241 (48), 235 (17), 223 (16), 207 (18), 205 (20), 200 (19), 199 (100), 197 (18), 193 (14), 189 (20), 183 (17), 181 (51), 177 (19), 167 (15), 165 (12), 163 (77), 161 (50), 157 (15), 139 (70), 135 (50), 129 (68), 121 (18), 115 (29), 105 (39), 101 (27), 91 (85), 85 (20), 79 (26), 77 (34), 73 (22), 69 (19), 59 (52), 57 (17), 55 (53); HRMS (ESI): Calcd for $C_{24}H_{32}O_5SiNa$ $[M+Na]^+$: 451.1911. Found: 451.1916.

To a solution of (3a*R*,6*R*,6a*R*)-6-((*tert*-butyldiphenylsilyloxy)-methyl)-2,2-dimethyl-tetrahydrofuro[3,4-d][1,3]dioxol-4-ol (465 mg, 1.1 mmol) in dry CH_2Cl_2 (11 mL) at 0 °C was added bromotrimethylsilane (0.43 mL, 3.3 mmol, 3 equiv). After 2 h at room temperature, the solvent was removed under reduced pressure, and the product was filtered through a short pad of silica gel (PE/EtOAc, 90/10) to yield **2** (281 mg, 0.57 mmol, 52%) which was directly engaged in the cross-coupling reaction: ^1H NMR (400 MHz, $CDCl_3$) δ 7.74−7.70 (m, 4H), 7.47−7.40 (m, 6H), 6.45 (s, 1H), 5.16 (d, *J* = 5.8 Hz, 1H), 4.88 (dd, *J* = 5.8, 1.6 Hz, 1H), 4.49 (ddd, *J* = 8.5, 6.1, 1.6 Hz, 1H), 4.04 (dd, *J* = 10.7, 8.5 Hz, 1H), 3.92 (dd, *J* = 10.7, 6.1 Hz, 1H), 1.50 (s, 3H), 1.36 (s, 3H), 1.13 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.7, 133.1, 133.0, 129.9, 128.4, 127.8, 113.5, 92.6, 90.9, 90.3, 81.3, 62.0, 26.9, 26.7, 25.5, 19.3.

***tert*-Butyl(((3a*R*,4*R*,6*S*,6a*S*)-2,2-dimethyl-6-phenyl-tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methoxy)diphenylsilane.** (from **2**, Table 1, entry 2) $[\alpha]_D^{20}$ −5.6 (*c* 1.0, $CHCl_3$); IR (neat): 3069, 2930, 2857, 1427, 1211, 1110, 1073, 860, 822, 737, 697, 610 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.67−7.62 (m, 4H), 7.38−7.17 (m, 11H), 4.84 (d, *J* = 5.3 Hz, 1H), 4.75 (dd, *J* = 6.7, 3.9 Hz, 1H), 4.47 (dd, *J* = 6.7, 5.4 Hz, 1H), 4.14 (q, *J* = 3.9 Hz, 1H), 3.88 (dd, *J* = 11.2, 3.9 Hz, 1H), 3.81 (dd, *J* = 11.2, 3.9 Hz, 1H), 1.56 (s, 3H), 1.29 (s, 3H), 1.00 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.1, 135.8, 133.4, 129.9, 129.8, 128.5, 127.8, 125.9, 114.6, 87.2, 85.2, 84.5, 81.7, 64.1, 27.8, 26.9, 25.7, 19.4; MS (EI) *m*/*z*: 373 (14), 295 (23), 242 (10), 241 (43), 223 (11), 217 (12), 199 (29), 189 (10), 163 (54), 162 (12), 161 (90), 143 (20), 139 (27), 135 (25), 133 (10), 129 (11), 115 (12), 105 (30), 103 (69), 91 (100), 77 (26), HRMS (ESI): Calcd for $C_{30}H_{36}O_4SiNa$ $[M+Na]^+$: 511.2275. Found: 511.2274.

((3a*R*,4*R*,6a*R*)-6-Bromo-2,2-dimethyl-tetrahydrofuro[3,4-d]-[1,3]dioxol-4-yl)methyl benzoate (3). To a solution of (3a*R*,6*R*,6a*R*)-6-(Hydroxymethyl)-2,2-dimethyl-tetrahydrofuro[3,4-*d*]-[1,3]dioxol-4-ol[29] (1.11 g, 5.84 mmol) in dry pyridine (5.8 mL), was added 1.1 equiv of benzoyl chloride (903 mg, 0.75 mL, 6.42 mmol). The reaction was stirred at room temperature overnight. The reaction was quenched with water and extracted with CH_2Cl_2. The organic layer was washed with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the product was purified by silica-gel chromatography (PE/EtOAc, 80/20) to yield ((3a*R*,4*R*,6a*R*)-6-Hydroxy-2,2-dimethyl-tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl benzoate as a 66:33 mixture of α- and β-isomers (791 mg, 2.7 mmol, 46%): IR (neat): 3434, 2987, 2941, 1719, 1451, 1374, 1269, 1067, 1026, 867, 709 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (dd, *J* = 8.3, 1.2 Hz, 1.32H), 7.98 (dd, *J* = 8.3, 1.2 Hz, 0.66H), 7.60−7.53 (m, 1H), 7.47−7.40 (m, 2H), 5.51 (s, 0.33H), 5.49 (brs, 0.66H), 4.80 (brd, *J* = 6.0 Hz, 0.66H), 4.76 (dd, *J* = 6.3, 1.5 Hz, 0.33H), 4.69 (d, *J* = 6.0 Hz, 0.66H), 4.67 (m, 0.33H), 4.56−4.5 (m, 1.32H), 4.46−42 (m, 0.66H), 4.39−4.32 (m, 1H), 4.04 (brs, 0.33H), 3.71 (brs, 0.66H), 1.58 (s, 1H), 1.48 (s, 2H), 1.38 (s, 1H), 1.33 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 166.2, 133.5, 133.3, 129.9, 129.7, 129.7, 129.5, 128.7, 128.5, 114.2, 112.8, 103.2, 97.6, 86.0, 87.9, 82.1, 82.1, 79.3, 78.7, 65.8, 65.7, 26.6, 26.2, 25.1, 24.9; MS (EI) *m*/*z*: 279 ($[M-Me]^+$, 7), 114 (15), 113 (7), 106 (8), 105 (100), 86 (6), 85 (7), 77 (28), 69 (11), 68 (18), 59 (24), 51 (7); HRMS (ESI): Calcd for $C_{15}H_{18}O_6Na$ $[M+Na]^+$: 317.0996. Found: 317.0997. To a solution of ((3a*R*,4*R*,6a*R*)-6-Hydroxy-2,2-dimethyl-tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl benzoate (791 mg, 2.7 mmol) in dry CH_2Cl_2 (27 mL) at 0 °C was added 3 equiv of bromotrimethylsilane (1.06 mL, 8.1 mmol). The reaction was stirred at room temperature during 2 h. The solvent was removed under reduced pressure, and the product was purified over a short pad of silica gel (PE/EtOAc, 90/10) to yield **3** as a 85:15 mixture of α- and β-isomers (142 mg, 0.41 mmol, 15%) which was directly engaged in the cross-coupling reaction: ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.5, 2H), 7.58 (t, *J* = 8.5, 1H), 7.45 (t, *J* = 8.5, 2H), 6.48 (s, 0.85H), 5.54 (s, 0.15H), 5.28 (d, *J* = 5.8 Hz, 0.85H), 4.98 (dd, *J* = 5.8, 1.4 Hz, 0.85H), 4.81 (dd, *J* = 5.8, 1.4 Hz, 0.15H), 4.72−4.67 (m, 1.7H), 4.61 (m, 0.15H), 4.60 (dd, *J* = 14.3, 9.5 Hz, 0.85H) 4.49 (m, 0.15H), 4.38 (dd, *J* = 6.8, 3.0 Hz, 0.15H), 1.50 (s, 0.45H), 1.48 (s, 2.55H), 1.35 (s, 2.55H), 1.33 (s, 0.45H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (α-isomer): 166.2, 133.4, 130.0, 129.6, 128.6, 114.0, 91.9, 90.5, 88.3, 81.5, 62.7, 26.8, 25.5.

((3a*R*,4*R*,6*S*,6a*S*)-2,2-Dimethyl-6-phenyl-tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl benzoate. (from **3**, Table 1, entry 3) $[\alpha]_D^{20}$ −42.8 (*c* 0.95, $CHCl_3$); IR (neat): 3033, 2987, 2937, 1720, 1451, 1373, 1267, 1211, 1070, 1025, 859, 709, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.94 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.50 (tt, *J* = 8.3, 1,4 Hz, 1H), 7.38−7.32 (m, 4H), 7.28−7.23 (m, 2H), 7.22−7.18 (m, 1H), 4.94 (d, *J* = 5.0 Hz, 1H), 4.69 (dd, *J* = 6.8, 4.2 Hz, 1H), 4.57 (dd, *J* = 11.8, 3.8 Hz, 1H), 4.56 (dd, *J* = 6.8, 5.0 Hz, 1H), 4.48 (dd, *J* = 11.8, 4.5 Hz, 1H), 4.39 (brq, *J* = 4.0 Hz, 1H), 1.58 (s, 3H), 1.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 139.7, 133.3, 129.8, 128.7, 128.6, 128.0, 125.7, 115.1, 87.3, 86.1, 82.2, 82.0, 64.7, 27.7, 25.7; MS (EI) *m*/*z*: 339 ($[M-Me]^+$, 1), 174 (34), 157 (8), 131 (9), 106 (9), 105 (100), 91 (9), 77 (32), 69 (29), 68 (44); HRMS (ESI): Calcd for $C_{21}H_{22}O_5Na$ $[M+Na]^+$: 377.1359. Found: 377.1362.

(((3a*S*,4*R*,6a*S*)-6-Bromo-2,2-dimethyl-tetrahydrofuro[3,4-d]-[1,3]dioxol-4-yl)methoxy)(*tert*-butyl)diphenylsilane (4). To a solution of (3a*S*,6*R*,6a*S*)-6-(Hydroxymethyl)-2,2-dimethyl-tetrahydrofuro[3,4-d][1,3]dioxol-4-ol[30] (468 mg, 2.46 mmol) and imidazole (427 mg, 6.9 mmol, 2.8 equiv) in dry DMF (1.2 mL), was added *tert*-butyl(chloro)diphenylsilane (744 mg, 0.7 mL, 2.7 mmol, 1.1 equiv). After 2 h at room temperature, the reaction was quenched with water and extracted with CH_2Cl_2. The organic layer was washed with

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brine and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the product was purified by silica gel chromatography (CH_2Cl_2/MeOH 95/5) to yield (3a*S*,6*R*,6a*S*)-6-((*tert*-Butyldiphenylsilyloxy)methyl)-2,2-dimethyl-tetrahydrofuro[3,4-d]-[1,3]dioxol-4-ol as a 78:22 mixture of α- and β-isomers (498 mg, 1.16 mmol, 47%): IR (neat): 3422, 3071, 2933, 2857, 1427, 1373, 1209, 1086, 998, 823, 803, 740, 701, 613 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.73−7.69 (m, 4H), 7.44−7.35 (m, 6H), 5.38 (s, 0.78H), 4.98 (brd, J = 8.0 Hz, 0.22H), 4.75 (dd, J = 5.9, 3.6 Hz, 0.78H), 4.73 (dd, J = 6.3, 3.5 Hz, 0.22H), 4.58 (d, J = 5.9 Hz, 0.78H), 4.49 (dd, J = 6.3, 3.5 Hz, 0.22H), 4.33 (m, 0.78H), 3.99 (dd, J = 10.5, 5.5 Hz, 0.78H), 3.98 (dd, J = 10.1, 7.3 Hz, 0.22H), 3.91 (dd, J = 10.1, 5.4 Hz, 0.22H), 3.90 (dd, J = 10.5, 6.8 Hz, 0.78H), 3.69 (ddd, J = 7.3, 5.4, 3.5 Hz, 0.22H), 1.45 (s, 0.66H), 1.36 (s, 3H), 1.32 (s, 2.07H), 1.28 (s, 2.34H), 1.06 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.8, 133.7, 129.8, 129.7, 127.8, 127.7, 113.1, 112.6, 101.4, 96.9, 85.6, 81.1, 79.9, 79.5, 78.3, 76.3, 62.1, 61.4, 26.9, 26.2, 25.9, 25.2, 25.1, 19.4; MS (EI) m/z: 413 ([M-Me]$^+$, 4), 371 (10), 283 (16), 257 (29), 253 (12), 241 (41), 235 (34), 223 (19), 207 (23), 205 (26), 200 (18), 199 (92), 197 (20), 193 (30), 189 (25), 183 (18), 181 (41), 177 (32), 167 (14), 163 (100), 161 (24), 157 (17), 139 (80), 135 (53), 133 (15), 129 (63), 123 (14), 121 (19), 119 (26), 117 (20), 115 (43), 105 (47), 103 (11), 101 (46), 91 (86), 85 (13), 79 (32), 78 (12), 77 (40), 73 (14), 69 (14), 59 (54), 57 (21), 55 (51); HRMS (ESI): Calcd for $C_{24}H_{32}O_5SiNa$ [M+Na]$^+$: 451.1911. Found: 451.1912. To a solution of (3a*S*,6*R*,6a*S*)-6-((*tert*-Butyldiphenylsilyloxy)methyl)-2,2-dimethyl-tetrahydrofuro[3,4-d][1,3]dioxol −4-ol (236 mg, 0.55 mmol) in dry CH_2Cl_2 (5.5 mL) at 0 °C was added bromo-trimethylsilane (0.15 mL, 1.1 mmol, 2 equiv). After 2 h at room temperature, the solvent was removed under reduced pressure, and the product was eluated through a pad of silica gel (PE/Et_2O, 90/10) to yield **4** which was directly engaged in the cross-coupling step: (174 mg, 0.26 mmol, 64%): ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (t, J = 8.1 Hz, 4H), 7.45−7.37 (m, 6H), 6.44 (s, 1H), 5.16 (d, J = 5.8 Hz, 1H), 4.84 (dd, J = 5.8, 3.6 Hz, 1H), 4.42 (ddd, J = 6.6, 5.9, 3.6 Hz, 1H), 4.06 (dd, J = 10.7, 5.9 Hz, 1H), 3.92 (dd, J = 10.7, 6.6 Hz, 1H), 1.33 (s, 3H), 1.30 (s, 3H), 1.08 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ: 135.8, 133.4, 133.3, 129.8, 127.8, 113.2, 93.8, 90.1, 94.0, 78.4, 60.7, 26.9, 26.1, 25.3, 19.4; MS (EI) m/z: 337 (3), 295 (11), 209 (7), 208 (12), 206 (61), 115 (5), 74 (8), 73 (100).

***tert*-Butyl(((3a*S*,4*R*,6*R*,6a*R*)-2,2-dimethyl-6-phenyl-tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methoxy)diphenylsilane.** (from **4**, Table 1, entry 4) $[\alpha]_D^{20}$ +6.5 (*c* 1.05, $CHCl_3$); IR (neat): 3070, 2931, 2857, 1427, 1371, 1209, 1141, 1090, 1001, 823, 805, 739, 700, 613 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ: 7.66−7.63 (m, 4H), 7.33−7.25 (m, 10H), 7.20−7.16 (m, 1H), 5.07 (brs, J = 5.3 Hz, 1H), 4.82 (dd, J = 6.0, 1.0 Hz, 1H), 4.47 (brd, J = 6.0 Hz, 1H), 3.99−3.93 (m, 3H), 1.39 (s, 3H), 1.25 (s, 3H), 1.00 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9, 135.7, 133.7, 133.6, 129.6, 128.6, 127.7, 127.6, 127.3, 125.5, 112.7, 87.6, 84.7, 81.6, 81.2, 62.1, 26.9, 26.4, 25.3, 19.3; MS (EI) m/z: 473 ([M-Me]$^+$, 1), 317 (15), 295 (12), 241 (26), 199 (22), 193 (14), 191 (13), 163 (37), 161 (73), 143 (16), 139 (20), 135 (18), 133 (28), 117 (11), 115 (14), 105 (28), 103 (68), 91 (100), 77 (22), HRMS (ESI): Calcd for $C_{30}H_{36}O_4SiNa$ [M+Na]$^+$: 511.2275. Found: 511.2272.

((3a*S*,4*R*,6*R*,6a*S*)-6-Bromo-2,2-dimethyl-tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl benzoate (5). To a solution of (3a*S*,6*R*,6a*S*)-6-(Hydroxymethyl)-2,2-dimethyl-tetrahydrofuro[3,4-d]-[1,3]dioxol-4-ol[30] (310 mg, 1.6 mmol) in dry pyridine (3.2 mL), was added benzoyl chloride (252 mg, 0.21 mL, 1.8 mmol, 1.1 equiv). The reaction was stirred at room temperature for 4 h. Benzoyl chloride 0.26 equiv (0.05 mL) was added to the medium. After one night at room temperature, the reaction was quenched with water and extracted with CH_2Cl_2. The organic layer was washed with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the product was purified by silica gel chromatography (PE/EtOAc, 80/20) to yield ((3a*S*,4*R*,6a*S*)-6-hydroxy-2,2-dimethyl-tetrahydrofuro[3,4-d]-[1,3]dioxol-4-yl)methyl benzoate as a 78:22 mixture of α and β isomers (233 mg, 0.79 mmol, 49%): IR (neat): 3434, 2988, 2941, 1718, 1269, 1209, 1097, 1069, 1026, 999, 861, 708 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.10−8.04 (m, 2H), 7.62−7.54 (m, 1H), 7.48−7.41 (m, 2H), 5.48 (s, 0.78H), 5.05 (brd, J = 11.8 Hz, 0.22H), 4.87 (dd, J = 5.9, 3.6 Hz, 0.78H), 4.79 (dd, J = 6.0, 3.5 Hz, 0.22H), 4.71 (dd, J = 11.2, 3.1 Hz, 0.78H), 4.69 (m, 0.22H), 4.66 (d, J = 6.0 Hz, 0.78H), 4.57−4.45 (m, 2H), 3.92 (ddd, J = 7.4, 4.2, 3.3 Hz, 0.22H), 1.55 (s, 0.66H), 1.48 (s, 2.34H), 1.38 (s, 0.66H), 1.33 (s, 2.34H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 166.6, 133.8, 133.2, 130.3, 130.0, 129.9, 128.6, 128.5, 113.7, 113.1, 101.6, 97.2, 85.6, 80.0, 79.8, 78.7, 78.4, 73.9, 63.4, 63.0, 26.2, 26.0, 25.1, 24.9; MS (EI) m/z: 279 ([M-Me]$^+$, 6), 114 (7), 113 (7), 106 (8), 105 (100), 85 (6), 77 (25), 68 (18), 59 (24), 51 (6); HRMS (ESI): Calcd for $C_{15}H_{18}O_6Na$ [M+Na]$^+$: 317.0996. Found: 317.0996. To a solution of ((3a*S*,4*R*,6a*S*)-6-hydroxy-2,2-dimethyl-tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl benzoate (233 mg, 0.79 mmol) in dry CH_2Cl_2 (8 mL) at 0 °C was added bromotrimethylsilane (0.21 mL, 1.6 mmol, 2 equiv). The reaction was stirred at room temperature for 2 h. The solvent was removed under reduced pressure, and the product was eluated through a short pad of silica gel (PE/Et_2O, 90/10) to yield **5** (122 mg, 0.34 mmol, 43%) which was directly engaged in the cross-coupling reaction: IR (neat): 2989, 1720, 1267. 1210, 1097, 1072, 857, 710, 688, 637 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 8.3 Hz, 2H), 7.58 (t, J = 8.3 Hz, 1H), 7.45 (t, J = 8.3 Hz, 2H), 6.47 (s, 1H), 5.19 (d, J = 5.8 Hz, 1H), 4.95 (dd, J = 5.8, 3.7 Hz, 1H), 4.77 (dd, J = 11.5, 3.5 Hz), 4.59 (m, 1H), 4.53 (dd, J = 11.5, 7.4 Hz, 1H), 1.47 (s, 3H), 1.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 133.4, 130.0, 129.8, 128.6, 113.7, 92.8, 90.1, 81.5, 78.6, 61.8, 26.1, 25.1; MS (EI) m/z: 443 ([M(^{81}Br)-Me]$^+$, 4), 441 ([M(^{79}Br)-Me]$^+$, 5), 277 (5), 160 (6), 158 (7), 106 (8), 105 (100), 97 (5), 77 (28), 69 (7), 68 (8), 59 (7), 51 (8).

((3a*S*,4*R*,6*R*,6a*R*)-2,2-Dimethyl-6-phenyl-tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl benzoate. (from **5**, Table 1, entry 5) $[\alpha]_D^{20}$ −18.6 (*c* 1.1, $CHCl_3$); IR (neat): 3062, 2988, 2938, 2872, 1720, 1270, 1209, 1105, 1070, 1027, 862, 711 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (dd, J = 8.4, 1.3 Hz, 2H), 7.58 (tdd, J = 8.3, 6.7, 1.3 Hz, 1H), 7.27 (t, J = 8.3 Hz, 2H), 7.19 (d, J = 4.5 Hz, 4H), 7.12−7.08 (m, 1H), 5.10 (brs, 1H), 4.82 (dd, J = 6.0, 1.2 Hz, 1H), 4.64 (dd, J = 6.0, 4.0 Hz, 1H), 4.58 (dd, J = 11.7, 4.4 Hz, 1H), 4.43 (dd, J = 11.7, 7.3 Hz, 1H), 4.14 (ddd, J = 7.3, 4.4, 4.0 Hz, 1H), 1.43 (s, 3H), 1.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 138.4, 133.1, 130.1, 129.8, 128.8, 128.4, 127.6, 125.6, 113.3, 87.5, 84.9, 81.3, 78.7, 63.5, 26.4, 25.1; MS (EI) m/z: 339 ([M-Me]$^+$, 1), 174 (6), 157 (9), 131 (8), 106 (9), 105 (100), 77 (31), 69 (26), 68 (47), 58 (5), 51 (6); HRMS (ESI): Calcd for $C_{21}H_{22}O_5Na$ [M+Na]$^+$: 377.1359. Found: 377.1361.

(3a*S*,4*R*,6*R*,6a*R*)-4-((*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyl-6-phenyl-tetrahydrofuro[3,4-d][1,3]dioxole (10).[31] (from **6**, Table 1, entry 6, Scheme 1) $[\alpha]_D^{20}$ −1.6 (*c* 0.8, $CHCl_3$); mp = 122−124 °C; IR (neat): 2986, 2934, 2878, 1603, 1495, 1449, 1371, 1257, 1208, 1160, 1118, 1064, 977, 891, 846, 734, 699 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 7.23 (d, J = 8.3 Hz, 2H), 7.10 (t, J = 8.3 Hz, 2H), 7.03 (d, J = 8.3 Hz, 1H), 5.26 (brs, 1H), 4.65 (dd, J = 12.6, 6.6 Hz, 1H), 4.61 (dd, J = 6.6, 1.3 Hz, 1H), 4.32 (m, 2H), 4.20 (dd, J = 8.6, 6.6 Hz, 1H), 3.96 (dd, J = 6.6, 3.6 Hz, 1H), 1.47 (s, 6H), 1.34 (s, 3H), 1.16 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 139.6, 128.9, 127.5, 125.8, 112.7, 109.1, 88.2, 85.6, 82.2, 81.6, 74.1, 67.4, 27.1, 26.5, 25.7, 24.9; MS (EI) m/z: 305 ([M-Me]$^+$, 25), 187 (10), 145 (10), 141 (13), 131 (17), 115 (15), 107 (7), 105 (22), 103 (19), 101 (100), 99 (12), 98 (11), 91 (35), 85 (7), 83 (8), 81 (10), 78 (7), 77 (21), 73 (21), 72 (17), 70 (10), 69 (7), 68 (20), 59 (24), 55 (11).

***α*-1′,2′-Dideoxy-3′,5′-di-*O*-toluoyl-1′-(3-phenyl)-ribofuranose.**[32] (from **7**, Table 1, entry 7) $[\alpha]_D^{20}$ +5.3 (*c* 1.5, $CHCl_3$); IR (neat): 3032, 2951, 1712, 1611, 1266, 1177, 1102, 1019, 839, 751, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 8.3 Hz, 2H), 7.71 (d, J = 8.3 Hz, 2H), 7.46 (d, J = 7.5 Hz, 2H), 7.39 (t, J = 7.5 Hz, 2H), 7.31 (t, J = 7.5 Hz, 1H), 7.26 (d, J = 8.0 Hz, 2H), 7.20 (d, J = 8.0 Hz, 2H), 5.64 (ddd, J = 6.8, 3.7, 3.0 Hz, 1H), 5.35 (dd, J = 7.1, 6.1 Hz, 1H), 4.80 (dd, J = 4.8, 3.0 Hz, 1H), 4.64 (dd, J = 11.8, 4.8 Hz, 1H), 4.62 (dd, J = 11.7, 4.8 Hz, 1H), 2.84 (ddd, J = 13.7, 7.1, 6.8 Hz, 1H), 2.44 (s, 3H), 2.42 (s, 3H), 2.36 (ddd, J = 13.7, 6.1, 3.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 166.2, 144.0, 143.9, 142.5, 129.9, 129.8, 129.3, 129.1, 128.5, 127.5, 127.2, 126.9, 125.7, 82.2, 80.3,

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76.5, 64.7, 40.5, 21.8; MS (EI) *m/z*: 274 (11), 198 (7), 197 (48), 196 (6), 183 (9), 169 (12), 168 (16), 165 (9), 154 (6), 119 (39), 106 (8), 105 (100), 91 (24), 77 (54), 65 (9), 51 (10).

(3*aS*,4*R*,6*R*,6*aR*)-4-((*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl)-6-(4-fluorophenyl)-2,2-dimethyl-tetrahydrofuro[3,4-d][1,3]dioxole. (from **6**, Table 2, entry 1) $[\alpha]_D^{20}$ +18.0 (*c* 0.9, $CHCl_3$); IR (neat): 2986, 2937,1606, 1508, 1371, 1256, 1209, 1158, 1118, 1064, 1013, 978, 896, 841 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.27 (dd, *J* = 8.9, 5.3 Hz, 2H), 7.03 (tapp, *J* = 8.9 Hz, 2H), 5.13 (brs, 1H), 4.91 (brd, *J* = 6.0 Hz, 1H), 4.75 (dd, *J* = 6.0, 3.8 Hz, 1H), 4.48 (dd, 7.3, 5.4 Hz, 1H), 4.16 (d, *J* = 5.4 Hz, 2H), 3.83 (dd, *J* = 7.3, 3.8 Hz, 1H), 1.55 (s, 3H), 1.42 (s, 3H), 1.37 (s, 3H), 1.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2 (d, J^1_{C-F} = 244 Hz), 134.2 (d, J^4_{C-F} = 3 Hz), 127.2 (d, J^3_{C-F} = 8 Hz), 115.6 (d, J^2_{C-F} = 21 Hz), 113.0, 109.3, 87.5, 84.6, 81.4, 81.2, 73.6, 67.0, 27.0, 26.3, 25.2, 24.8; MS (EI) *m/z*: 324 (5), 323 ([M-Me]$^+$, 29), 205 (10), 163 (7), 149 (8), 141 (10), 133 (5), 125 (5), 123 (12), 121 (8), 109 (22), 102 (6), 101 (100), 99 (10), 98 (10), 85 (5), 83 (7), 81 (14), 73 (13), 72 (15), 70 (8), 69 (5), 68 (15), 59 (18); HRMS (ESI): Calcd for $C_{18}H_{23}FNaO_5$ [M+Na]$^+$: 361.1422. Found: 361.1422.

(3a*S*,4*R*,6*S*,6a*S*)-4-((*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyl-6-(thiophen-2-yl)-tetrahydrofuro[3,4-d][1,3]-dioxole.[33] (from **6**, Table 2, entry 2). $[\alpha]_D^{20}$ +32.4 (*c* 1.2, $CHCl_3$); IR (neat): 2928, 1410, 1311, 1207, 1083, 1018, 970, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.27 (brd, *J* = 5.0 Hz, 1H), 6.99 (dd, *J* = 5.0, 3.5 Hz, 1H), 6.95 (dt, *J* = 3.5, 1.2 Hz, 1H), 5.32 (brs, 1H), 5.02 (brd, *J* = 5.9 Hz, 1H), 4.82 (dd, *J* = 5.9, 3.6 Hz, 1H), 4.45 (ddd, *J* = 7.5, 6.2, 4.5 Hz, 1H), 4.14 (dd, *J* = 8.7, 6.2 Hz, 1H), 4.09 (dd, *J* = 8.7, 4.5 Hz, 1H), 3.88 (dd, *J* = 7.5, 3.6 Hz, 1H), 1.55 (s, 3H), 1.42 (s, 3H), 1.38 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.3, 127.3, 125.5, 124.7, 113.1, 109.4, 86.8, 82.2, 81.4, 81.2, 73.3, 67.2, 27.0, 26.2, 25.3, 24.9; MS (EI) *m/z*: 234 (9), 217 (6), 175 (6), 141 (11), 137 (21), 136 (100), 145 (45), 121 (34), 101 (62), 99 (8), 98 (12), 91 (7), 81 (11), 77 (10), 73 (12), 72 (13), 68 (16), 59 (14), 55 (8); HRMS (ESI): Calcd for $C_{16}H_{22}O_5SNa$ [M+Na]$^+$: 349.1080. Found: 349.1079.

(3a*S*,4*R*,6*R*,6a*R*)-4-((*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyl-6-(2-methylprop-1-enyl)-tetrahydrofuro[3,4-d][1,3]-dioxole. (from **6**, Table 2, entry 3) $[\alpha]_D^{20}$ +23.1 (*c* 1.29, $CHCl_3$); mp = 66−67 °C; IR (neat): 2985, 2935, 1671, 1454, 1371, 1256, 1208, 1161, 1116, 1064, 974, 942, 890, 849 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 5.07 (m, 1H), 4.89 (brd, *J* = 8.0, Hz, 1H), 4.63 (brq, *J* = 5.9 Hz, 1H), 4.50 (dd, *J* = 5.9, 3.6 Hz, 1H), 4.28 (dd 5.9, 0.8 Hz, 1H), 4.23 (dd, *J* = 8.4, 5.8 Hz, 1H), 4.02 (dd, *J* = 8.4, 6.4 Hz, 1H), 3.86 (dd, *J* = 6.9, 3.5 Hz, 1H), 1.49 (s, 3H), 1.48 (s, 3H), 1.48 (s, 6H), 1.33 (s, 3H), 1.17 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 136.7, 122.5, 112.5, 109.1, 87.3, 82.2, 81.4, 74.1, 67.5, 27.2, 26.5, 25.7, 25.0, 18.3; MS (EI) *m/z*: 283 ([M-Me]$^+$, 25), 181 (6), 165 (11), 141 (32), 138 (11), 111 (11), 101 (100), 99 (27), 98 (32), 87 (19), 95 (30), 93 (10), 85 (45), 83 (52), 81 (42), 79 (10), 73 (16), 72 (26), 70 (21), 69 (35), 68 (38), 67 (11), 59 (36), 55 (25), 53 (13); HRMS (ESI): Calcd for $C_{16}H_{26}NaO_5$ [M+Na]$^+$: 321.1672. Found: 321.1668.

(*R*)-1-((3a*S*,4*R*,6*R*,6a)-2,2-Dimethyl-6-phenyl-tetrahydrofuro-[3,4-d][1,3]dioxol-4-yl)ethane-1,2-diol (12). To a solution of **10** (804 mg, 2.5 mmol) in acetonitrile (25 mL) were added $BiCl_3$ (40 mg, 0.13 mmol, 5 mol %) and water (0.1 mL). The reaction was stirred at room temperature for 1 h, and then the solvent was removed under reduced pressure. Purification by silica gel chromatography (PE/EtOAc, 60/40 to 50/50) yielded the desired diol **12** (388 g, 1.39 mmol, 55%).[33b] $[\alpha]_D^{20}$ +20.6 (*c* 1.1, $CHCl_3$); IR (neat): 3421, 3061, 2935, 2872, 1373, 1260, 1208, 1083, 1048, 1026, 979, 887, 857, 803, 737, 702 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 7.33 (d, *J* = 8.1 Hz, 2H), 7.23 (t, *J* = 8.1 Hz, 2H), 7.13 (t, *J* = 8.1 Hz, 1H), 5.35 (brs, 1H), 4.72 (brd, *J* = 5.8 Hz, 1H), 4.57 (dd, *J* = 5.8, 3.7 Hz, 1H), 4.38 (m, 1H), 4.14 (dd, *J* = 11.5, 3.3 Hz, 1H), 4.07 (dd, *J* = 8.6, 3.7 Hz, 1H), 4.03 (dd, *J* = 11.5, 5.8 Hz, 1H), 3.72 (brs, 1H), 3.23 (brs, 1H), 1.60 (s, 3H), 1.31 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 139.4, 128.8, 127.5, 125.8, 112.9, 88.0, 85.4, 81.9, 81.0, 70.7, 64.9, 26.5, 25.1; MS (EI) *m/z*: 265 ([M-Me]$^+$, 11), 162 (12), 161 (10), 145 (29), 133 (34), 132 (15), 131 (44), 120 (18), 117 (11), 115 (18), 113 (14), 107 (100), 105 (67), 103 (30), 98 (21), 91 (80), 86 (77), 85 (16), 82 (20), 79 (34), 78 (13), 77 (44), 71 (11), 59 (97), 57 (39), 55 (20); HRMS (ESI): Calcd for $C_{15}H_{20}O_5Na$ [M+Na]$^+$: 303.1202. Found: 303.1202.

(*Z*)-Methyl-3-((3a*S*,4*R*,6*R*,6a*R*)-2,2-dimethyl-6-phenyl-tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)acrylate (14). To a solution of **12** (388 mg, 1.39 mmol) in THF (7.5 mL) and pH7 phosphate buffer solution (7.5 mL) was added $NaIO_4$ (0.89 g, 4.17 mmol, 3 equiv). The reaction was stirred at room temperature for 1 h, filtered over a short pad of Celite and extracted with EtOAc. The organic layer was dried over $MgSO_4$, and the solvent was removed under reduced pressure to provide aldehyde **13** which was not purified and used directly in the next step. To a solution of 18-crown-6 ether (1.62 g, 6.12 mmol, 4.4 equiv) and methyl 2-(bis(2,2,2-trifluoro-ethoxy)-phosphoryl)acetate **I** (0.58 mL, 2.78 mmol, 2 equiv) in dry THF (22 mL) at −78 °C was added 2.2 equiv of potassium bis(trimethylsilyl)-amide (6 mL, 0.5 M in toluene). The reaction mixture was stirred for 5 min, and aldehyde **13** in dry THF (2 mL) was added via cannula. After 1.5 h at −78 °C, the reaction was quenched with NH_4Cl saturated solution, warmed up to room temperature, and extracted with Et_2O. The organic layer was washed with brine and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the product was purified by silica gel chromatography (PE/Et_2O, 95/5) to yield the α,β-unsaturated ester **14** (214 mg, 0.71 mmol, 51% after 2 steps).[33b] $[\alpha]_D^{20}$ −6.0 (*c* 0.1, $CHCl_3$); IR (neat): 2926, 2854, 1719, 1438, 1372, 1223, 1198, 1161, 1090, 1066, 1047, 857, 820, 746, 708 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 7.29 (d, *J* = 8.1 Hz, 2H), 7.10 (t, *J* = 8.1 Hz, 2H), 7.02 (t, *J* = 8.1 Hz, 1H), 6.60 (dd, *J* = 11.6, 6.6 Hz, 1H), 5.86 (dd, *J* = 11.6, 1.7 Hz, 1H), 5.77 (ddd, *J* = 6.6, 4.1, 1.7 Hz, 1H), 5.41 (brs, 1H), 4.98 (dd, *J* = 5.9, 4.1 Hz, 1H), 4.70 (brd, *J* = 5.9 Hz, 1H), 3.22 (s, 3H), 1.54 (s, 3H), 1.16 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 166.1, 147.0, 139.5, 128.8, 127.5, 125.9, 120.4, 112.7, 88.1, 85.7, 83.5, 78.7, 50.9, 26.7, 25.0; MS (EI) *m/z*: 305 ([M+H]$^+$,1), 289 ([M-Me]$^+$, 3), 197 (17), 187 (12), 161 (37), 140 (38), 132 (47), 131 (100), 125 (13), 121 (15), 115 (11), 111 (45), 108 (36), 107 (12), 105 (35), 104 (20), 103 (24), 98 (40), 91 (25), 83 (11), 81 (38), 78 (11), 77 (26), 59 (25), 55 (12), 53 (11); HRMS (ESI): Calcd for $C_{17}H_{20}O_5Na$ [M+Na]$^+$: 327.1203. Found: 327.1203.

(−)-Isoaltholactone.[31f,33b]**.** To a solution of **14** (31 mg, 0.1 mmol) in a 95:5 mixture of toluene/water (1.5 mL) was added a catalytic amount of paratoluenesulfonic acid. The reaction was stirred at 100 °C for 2.5 h. The reaction was diluted with water and extracted with CH_2Cl_2. The phases were separated and the organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure, to afford (−)-**8** without purification in quantitative yield: $[\alpha]_D^{20}$ −23.0 (*c* 0.15, EtOH); IR (neat): 3240, 2928, 1721, 1577, 1397, 1313, 1144, 1104, 1038, 1024, 760, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39−7.30 (m, 5H), 6.87 (dd, *J* = 10.0, 4.5 Hz, 1H), 6.20 (dd, *J* = 10.0, 0.7 Hz, 1H), 5.05 (t app, *J* = 5.5 Hz, 1H), 4.88 (m, 1H), 4.78 (d, *J* = 7.3 Hz, 1H), 4.27 (dd, *J* = 7.3, 5.5 Hz, 1H), 3.16 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 142.0, 138.6, 128.8, 128.4, 125.9, 123.1, 83.4, 78.7, 78.5, 67.9; MS (EI) *m/z*: 232 ($M^{+\bullet}$, 9), 136 (7), 107 (23), 98 (8), 97 (100), 95 (28), 91 (12), 79 (18), 77 (16), 69 (11); HRMS (ESI): Calcd for $C_{13}H_{12}O_4Na$ [M+Na]$^+$: 255.0628. Found: 255.0631.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^1H and ^{13}C NMR spectra of compounds **1**-**4**, cross-coupling products from Table 1 and Table 2, as well as compounds **12**, **14**, and (−)-**8** are provided. This material is available free of charge via the Internet at http://pubs.acs.org/.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Štanbaský, J.; Hocek, M.; Kočovsky, P. *Chem. Rev.* **2009**, *109*, 6729. (b) Wu, Q.; Simmons, C. *Synthesis* **2004**, 1533. (c) Hutlin, P. G. *Curr. Top. Med. Chem.* **2005**, *5*, 1299. (d) Zou, W. *Curr. Top. Med. Chem.* **2005**, *5*, 1363. (e) Compain, P.; Martin, O. R. *Bioorg. Med. Chem.* **2001**, *9*, 3077. (f) Nicotra, F. *Top. Curr. Chem.* **1997**, *187*, 55.

(2) (a) Bililign, T.; Griffith, B. R.; Thorson, J. S. *Nat. Prod. Rep.* **2005**, *22*, 742. (b) Wellington, K. W.; Benner, S. A. *Nucleosides Nucleotides Nucleic Acids* **2006**, *25*, 1309.

(3) For a review on modification of natural DNA see: (a) Nielsen, P. E. *Chem. Biodiversity* **2007**, *1*, 1996. For reviews on *C*-nucleosides, see: (b) Wang, L.; Schultz, P. G. *Chem. Commun.* **2002**, 1. (c) Henry, A. A.; Remesberg, F. E. *Curr. Opin. Chem. Bio.* **2003**, *7*, 727. (d) Kool, E. T.; Morales, J. C.; Guckian, K. M. *Angew. Chem, Int. Ed.* **2000**, *39*, 990. (e) Kool, E. T. *Acc. Chem. Res.* **2002**, *35*, 936.

(4) For examples, see: (a) Franchetti, P.; Cappellacci, L.; Griffantini, M.; Barzi, A.; Nocentini, G.; Yang, H. Y.; O'Connor, A.; Jayaram, H. N.; Carrell, C.; Golstein, B. M. *J. Med. Chem.* **1995**, *38*, 3829. (b) Walker, J. A.; Liu, W.; Wise, D. S.; Drach, J. C.; Towsend, J. C. *J. Med. Chem.* **1998**, *41*, 1236. (c) Brotschi, C.; Häberli, A.; Leumann, C. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 3012. (d) Cuppelotti, A.; Cho, Y.; Park, J.-S.; Strässler, C.; Kool, E. T. *Bioconjugate Chem.* **2005**, *16*, 528.

(5) For examples, see: (a) Lee, D. Y. W.; He, M. *Curr. Top. Med. Chem* **2005**, *5*, 1333. (b) Somsàk, L. *Chem. Rev.* **2001**, *101*, 81. (c) Du, Y.; Linharrdt, R. J. *Tetrahedron* **1998**, *54*, 9913. (d) Jaramillo, C.; Knapp, S. *Synthesis* **1994**, 1. (e) Levy, D. E. ; Tang, C., in *The Chemistry of C-glycosides*; Tetrahedron Organic Chemistry Series, Vol. *13*; Elsevier: Oxford, 1995. (f) Beau, J.-M.; Gallager, T. *Top. Curr. Chem.* **1997**, *187*, 1. (g) Choumane, M.; Banchet, A.; Probst, N.; Gérard, S.; Plé, K.; Haudrechy, A. *C. R. Chimie* **2011**, *14*, 235.

(6) For recent methods, see: (a) Zheng, J.; Vedachalam, S.; Xiang, S.; Liu, X.-W *Org. Lett.* **2011**, *13*, 42. (b) Li, G.; Xiong, D.-C.; Ye, X.-S. *Synlett* **2011**, 2410. (c) Andrew, R. S.; Becker, J.-J.; Gagné, M. R. *Angew. Chem., Int. Ed.* **2010**, *49*, 7274. (d) Kaliappan, K. P.; Subrahmanyam, A. V. *Org. Lett.* **2007**, *9*, 1121. (e) Martin, S. F. *Pure Appl. Chem.* **2003**, *75*, 63.

(7) Lemaire, S.; Houpis, I. N.; Xiao, T.; Li, J.; Digard, E.; Gozlan, C.; Liu, R.; Gavryushin, A.; Diene, C.; Wang, Y.; Farina, V.; Knochel, P. *Org. Lett.* **2012**, *14*, 1480.

(8) (a) Gong, H.; Andrews, R. S.; Zucharello, J. L.; Lee, S. J.; Gagné, M. R. *Org. Lett.* **2009**, *11*, 879. (b) Gong, H.; Sinisi, R.; Gagné, M. R. *J. Am. Chem. Soc.* **2007**, *129*, 1908. (c) Gong, H.; Gagné, M. R. *J. Am. Chem. Soc.* **2008**, *130*, 12177.

(9) (a) Wu, Q. P.; Simmons, C. *Synthesis* **2004**, 1533. For reviews on cross-coupling reactions of nucleosides, see: (b) Agrofoglio, L. A.; Gillaizeau, I.; Saito, Y. *Chem. Rev.* **2003**, *103*, 1875. (c) Hocek, M. *Eur. J. Org. Chem.* **2003**, 245.

(10) For addition of Grignard reagents to fluorofurans, see: Yokoyama, M.; Toyoshima, H.; Shimizu, M.; Mito, J.; Togo, H. *Synthesis* **1998**, 409.

(11) For addition of Grignard reagents to chlorofurans, see: (a) Crombie, L.; Wyvill, R. D. *J. Chem., Soc. Perkin Trans. 1* **1985**, 1971. (b) Doboszewski, B. *Nucleosides Nucleotides Nucleic Acid* **2009**, *28*, 875. (c) Hashmi, S. A. M.; Hu, X.; Immos, C. E.; Lee, S. J.; Grinstaff, M. W. *Org. Lett.* **2002**, *4*, 4571. (d) Hocek, M.; Pohl, R.; Klepetářová, B. *Eur. J. Org. Chem.* **2005**, 4525. (e) Ogawa, A. K.; Wu, Y.; McMinn, D. L.; Liu, J.; Schultz, P. G.; Romesberg, F. E. *J. Am. Chem. Soc.* **2000**, *122*, 3274. (f) Chen, D.-W.; Beuscher, A. E.; Stevens, R. C.; Lerner, R. A.; Janda, K. D. *J. Org. Chem.* **2001**, *66*, 1725. (g) Scheitzer, B. A.; Kool, E. T. *J. Org. Chem.* **1994**, *59*, 7238. (h) François, P.; Perilleux, D.; Kempener, Y.; Sonveaux, E. *Tetrahedron Lett.* **1990**, *31*, 6347.

(12) For addition of Grignard reagents to bromofurans, see: Corey, E. J.; Bakshi, R. K.; Shibata, S.; Chen, C.-P.; Singh, V. K. *J. Am. Chem. Soc.* **1987**, *109*, 7925.

(13) For the use of copper-catalyzed cross-coupling with halogenofurans, see: (a) Thompson, A. S.; Tschaen, D. M.; Simpson, P.; McSwine, D.; Russ, W.; Little, E. D.; Verhoeven, T. R.; Shinkai, I. *Tetrahedron* **1990**, *31*, 6953. (b) Thompson, A. S.; Tschaen, D. M.; Simpson, P.; McSwine, D. J.; Reamer, R. A.; Verhoeven, T. R.; Shinkai, I. *J. Org. Chem.* **1992**, *57*, 7044. (c) Hainke, S.; Sinkh, I.; Hemmings, J.; Seitz, O. *J. Org. Chem.* **2007**, *72*, 8811.

(14) For the addition of organocadmium reagents to halogenofurans, see: (a) Chaudhuri, N. C.; Kool, E. T. *Tetrahedron Lett.* **1995**, *35*, 1795. (b) Chaudhuri, N. C.; Kool, E. T. *Tetrahedron Lett.* **1995**, *35*, 4910. (c) Ren, R. X.-F.; Chaudhuri, N. C.; Paris, P. L.; Rumney, S.; Kool, E. T. *J. Am. Chem. Soc.* **1996**, *118*, 7671. (d) Chaudhuri, N. C.; Rem, R. X.-F.; Kool, E. T. *Synlett* **1997**, 341. (e) Singh, I.; Hecker, W.; Prasad, A. K.; Parmar, V. S.; Seitz, O. *Chem. Commun.* **2002**, 500. (f) Zhang, L.; Long, H.; Boldt, G. E.; Janda, K. D.; Schatz, G. C.; Lewis, F. D. *Org. Biomol. Chem.* **2006**, *4*, 314. (g) Jiang, Y. L.; Stivers, S. T. *Tetrahedron Lett.* **2003**, *44*, 4051. (h) Griesang, N.; Richert, C. *Tetrahedron Lett.* **2002**, *43*, 8755.

(15) (a) Rival, N.; Hazelard, D.; Hanquet, G.; Kreuzer, T.; Bensoussan, C.; Reymond, S.; Cossy, J.; Colobert, F. *Org. Biomol. Chem.* **2012**, *47*, 9418−9428. (b) Bensoussan, C.; Rival, N.; Hanquet, G.; Colobert, F.; Reymond, S.; Cossy, J. *Tetrahedron* **2013**, *69*, 7759.

(16) (a) Guérinot, A.; Reymond, S.; Cossy, J. *Angew. Chem., Int. Ed.* **2007**, *46*, 6521. (b) Anxionnat, B.; Guérinot, A.; Reymond, S.; Cossy, J. *Tetrahedron Lett.* **2009**, *50*, 3470. (c) Guérinot, A.; Serra-Muns, A.; Gnamm, C.; Bensoussan, C.; Reymond, S.; Cossy, J. *Org. Lett.* **2010**, *12*, 1808. (d) Guérinot, A.; Serra-Muns, A.; Bensoussan, C.; Reymond, S.; Cossy, J. *Tetrahedron* **2011**, *67*, 5024.

(17) (a) Nicolas, L.; Angibaud, P.; Stansfield, I.; Pascal, B.; Meerpoel, L.; Reymond, S.; Cossy, J. *Angew. Chem., Int. Ed.* **2012**, *51*, 11101. (b) Nicolas, L.; Butkevich, A.; Guérinot, A.; Corbu, A.; Reymond, S.; Cossy, J. *Pure Appl. Chem.* **2013**, *85*, 1203.

(18) See the experimental part for the preparation of the *C*-halogeno furanosides.

(19) Gao, M.; Chen, Y.; Tan, S.; Reibenspies, J. H.; Zingaro, R. A. *Heteroatom Chem.* **2008**, *19*, 199.

(20) Spencer, R. P.; Cavallero, C. L.; Schwartz, J. *J. Org. Chem.* **1999**, *64*, 3987.

(21) (a) Hoeffer, M. *Chem. Ber.* **1960**, *93*, 2777. (b) Hoeffer, M.; Dushinsky, R.; Fox, J. J.; Yung, N. *J. Am. Chem. Soc.* **1959**, *81*, 4112. (c) Wu, J. C.; Bazin, H.; Chattopadhyaya, J. *Tetrahedron* **1987**, *43*, 2355−2368. (d) Bobek, M.; Kavai, I.; De Clercq, E. *J. Med. Chem.* **1987**, *30*, 1494. (e) Rolland, V.; Kotera, M.; Lhomme, J. *Synth. Commun.* **1997**, *27*, 3505.

(22) (a) Loder, J. W.; Nearn, R. H. *Heterocycles* **1977**, *7*, 113. (b) El-Zayat, A. A. E.; Ferrigni, N. R.; McCloud, T. G.; McKenzie, A. T.; Byrn, S. R.; Cassady, J. M.; Chang, C. J.; McLaughlin, J. L. *Tetrahedron Lett.* **1985**, *26*, 955.

(23) Colegate, S. M.; Din, L. B.; Latiff, A.; Salleh, M.; Samsudin, M. W.; Skelton, B. W.; Tadano, K.-I.; White, A. H.; Zakaria, Z. *Phytochemistry* **1990**, *29*, 1701.

(24) Ueno, Y.; Tadano, K.; Ogawa, S.; McLaughlin, J. L.; Alkohafi, A. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 2328.

(25) (a) Chen, J. -L.; Chu, L.; Qing, F. -L. *J. Fluorine Chem.* **2013**, *152*, 70. (b) Moro, A. V.; Santos, M. R. D.; Correira, C. R. D. *Eur. J. Org. Chem.* **2011**, 7259.

(26) (a) Harris, J. M.; O'Doherty, G. A. *Org. Lett.* **2000**, *2*, 2983. (b) Harris, J. M.; O'Doherty, G. A. *Tetrahedron* **2001**, *57*, 5161. (c) Peng, X.; Li, A.; Lu, J.; Wang, Q.; Pan, X.; Chan, A. S. C. *Tetrahedron* **2002**, *58*, 6799. (d) Yadav, J. S.; Rajaiah, G.; Raju, A. K. *Tetrahedron* **2003**, *59*, 5831. (e) Yadav, J. S.; Raju, A. K.; Rao, P. R.; Rajaiah, G. *Tetrahedron: Asymmetry* **2005**, *16*, 3283. (f) Unsworth, W. P.; Stevens, K.; Lamont, S. G.; Robertson, J. *Chem. Commun.* **2011**, *47*, 7659.

(27) (a) Meira, P. R. R.; Moro, A. V.; Correira, C. R. D. *Synthesis* **2007**, 2279. (b) For a formal synthesis, see: Trost, B. M.; Aponick, A.; Stanzl, B. N. *Eur. J. Org. Chem.* **2011**, 7259.
(28) (a) From 2,3-*O*-cyclohexylidene-D-glyceraldehyde: Hiratate, A.; Kiyota, H.; Oritani, T. J. *Pestic. Sci.* **2001**, *26*, 61. (b) Very recently, form D-mannose: Liu, J.; Zhang, X.; Liu, Y.; Bi, J. J.; Du, Y. G. *Science China Chem.* **2013**, *56*, 928.
(29) Kaskar, B.; Heise, G. L.; Michalak, R. S.; Vishnuvajjala, B. R. *Synthesis* **1990**, 1031.
(30) Yow, F.; Cheng-Hua, S.; Yu-Ting, S.; Chung-Hsu, Y.; Jang-Feng, L.; Chun-Chen, L.; Rashmi, R.; Ching-Wu, H.; Hao-Ai, S. *Org. Biomol. Chem.* **2012**, *10*, 931.
(31) Shing, T. K. M.; Gillhouley, J. G. *Tetrahedron* **1994**, *50*, 8685.
(32) Chaudhuri, N. C.; Ren, R. X.-F.; Kool, E. T. *Synlett* **1997**, 341.
(33) Krishna, P. R.; Lavanya, B.; Ilangovan, A.; Sharma, G. V. M . *Tetrahedron: Asymmetry* **2000**, *11*, 4463.

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