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Stereodefined Access to 3-Deoxy Sugars Through a Tandem Baylis–Hillman and Lewis Acid Catalyzed Reaction Sequence

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An innovative synthetic protocol is reported for the ready access to 3-deoxy sugars in both D and L forms as exclusive products (des >95%) in high yields through a stereodefined Lewis acid catalyzed reaction sequence of the sugar-derived Baylis–Hillman adducts.

Introduction

It is well established that the Baylis–Hillman reaction efficiently converts simple starting materials into highly functionalized products,[1] that are versatile synthetic intermediates in organic synthesis.[2] Since the Baylis–Hillman reaction results in the creation of a new chiral centre, the asymmetric[3] version of this reaction has attracted much attention in recent years. Our own contributions in this area[4] led to reports on diastereoselective Baylis–Hillman reaction using sugar-derived aldehydes,[5] chiral 2,3-epoxy aldehydes[6] as novel electrophiles and sugar-derived auxiliary assisted strategies.[7] In addition, carbohydrates and carbohydrate-containing saturated moieties contribute to the general mechanism of action of many bio-active drugs. Also, deoxy sugars are frequently encountered as part of oligosaccharide moieties in glycoconjugates.[8] Deoxy and dideoxy sugars constitute important precursors for accessing modified nucleosides as potential antiviral agents for HIV and HBV.[9] Since these products would serve as valuable components in the synthesis of sugar-modified nucleosides, their syntheses assumed importance in antisense-based new drug discovery.[10] The number of carbohydrates available as suitable starting materials is rather restricted so that lengthy syntheses are required to selectively remove hydroxy group, important new functional groups or to switch from the D- into the L-series and/or vice versa.[8] These drawbacks can be overcome by total synthesis approaches using flexible methodologies that allow a high degree of stereoselection.[8] Classical synthesis of 3-deoxy sugars bank either on the deoxygenation strategy[11] or β-elimination followed by catalytic hydrogenation protocol.[12] Herein we report an innovative synthesis of 3-deoxy sugars **9** and **10** in both D and L forms as exclusive products (des >95%) in high yields through a sequential Baylis–Hillman reaction and Lewis acid catalyzed reaction.

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Results and Discussion

At the outset, when methyl 2,3-*O*-isopropylidene-β-D-*ribo*-pentodialdo-1,4-furanose (**1**) (Scheme 1) was subjected to conventional DABCO-catalyzed Baylis–Hillman reaction in 1,4-dioxane/water (1:1) at room temperature, it unusually resulted in a divinyl carbinol **1a** (Scheme 1, 64%). In the ^{1}H NMR spectrum, one of the two olefinic protons of the external double bond appeared at δ = 5.92 as a singlet for the major isomer while the same proton resonated at δ = 6.00 for the minor isomer with the same integral ratio; while the other olefinic proton resonated at δ = 6.32 for the minor isomer while the isomeric proton appeared at δ = 6.30 as singlet with the identical integral ratio. A new olefinic proton appeared at δ = 5.17 for the major isomer while for minor isomer at δ = 5.14 with a relative integration of 0.55:0.45 and the protons corresponding to the isopropylidene group were lost which made us to assign the structure as shown. Further support for the assigned structure was obtained from other analytical data viz. ^{13}C NMR, low- and high-resolution mass spectral analyses. We rationalized the product formation by the fact that the 2,3-isopropylidene group behaved as a leaving group to render the product, primarily due to the *syn*-relation of the functional group at C3 and H4.

To validate the above observation, we have selected two other aldehydes: namely 1,2-*O*-isopropylidene-3-*O*-tosyl-α-D-*ribo*-pentodialdo-1,4-furanose (**2**) and 1,2-*O*-isopropylidene-3-*O*-tosyl-β-D-*arabino*-pentodialdo-1,4-furanose (**3**)[13] with similar relative stereochemistry at C-3 and C-4 centers as of **1** and subjected them to Baylis–Hillman reaction with ethyl acrylate under the standardized conditions to result in the divinyl carbinols **2a** (80%) and **3a** (86%) respectively in

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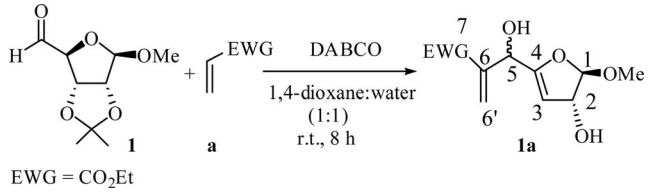
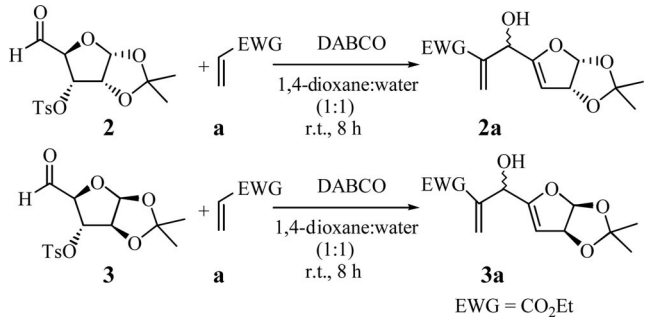
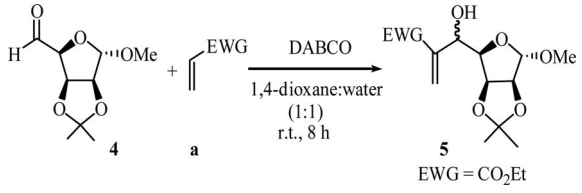


Scheme 1.

very good yields (Scheme 2). The structures of **2a** and **3a** were analogously proved based on their spectroscopic data. Thus, this kind of conversion is a general process with substrates suitably substituted with an *anti*-stereochemistry at the 3-position with respect to the aldehyde functionality. Conversely, when 2,3-*O*-isopropylidene-1-*O*-methyl-α-D-*lyxo*-pentodialdo-1,4-furanose (**4**) was utilized[5] in the Baylis–Hillman reaction, the normal adduct **5** was the sole product (Scheme 3).



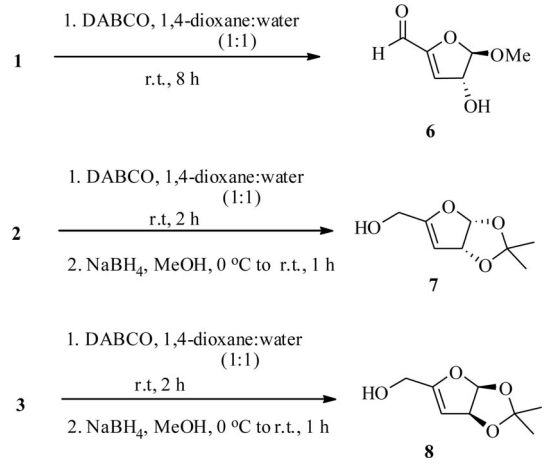
Scheme 2.



Scheme 3.

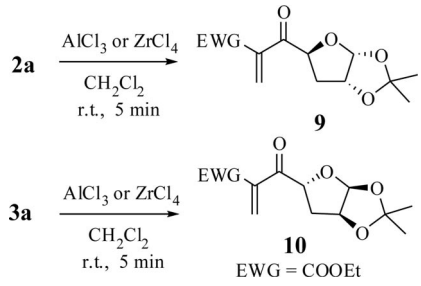
This result substantiates the fact that the stereochemical disposition of the C3 and H4 groups play a definite role either to provide a divinyl carbinol (Scheme 2) or the normal Baylis–Hillman adduct as the product (Scheme 3).

In order to validate the fact that the elimination of C-3 group takes place first, we performed blank reactions[14] of **1**, **2** and **3** in the presence of only base (DABCO) in dioxane/water and obtained the corresponding enals. Due to the instability of aldehydes derived from **2** and **3** we isolated their corresponding alcohols **7** and **8**, respectively, after $NaBH_4$ reduction (Scheme 4). From this investigation we concluded that the formation of enal is indeed the first step in the formation of divinyl carbinols.



Scheme 4.

Interestingly, divinyl carbinols constitute an important class of allylic alcohols.[15] The presence of two chemically distinctive double bonds in **2a** and **3a** will provide an ample opportunity to discriminate one from another, namely, the acid susceptible enolic double bond and the Michael addition prone active olefin. With a hope to extend the utility of these divinyl carbinols we expected a Nazarov cyclization with the oxidized form of **2a** and **3a**. All the attempts to obtain the divinyl ketones by the oxidation of **2a** and **3a** resulted in the corresponding unstable ketones.[16] As a consequence, we investigated the fate of compounds **2a** and **3a** themselves under Nazarov cyclization conditions; initially **2a** was subjected to a Lewis acid ($AlCl_3/CH_2Cl_2$/room temp./5 min) reaction. Surprisingly, a single product was isolated, which upon thorough characterization was assigned as **9** (85%, Scheme 5). For instance, the ^1H NMR spectrum of **9** revealed the olefinic protons at δ = 6.42 and 5.92 as singlets, H-1 appeared at δ = 5.72 as a doublet (J = 5.3 Hz) along with the allylic proton at its usual chemical shift. Though the absence of H-3 in the olefinic region was observed, but more importantly the same H-3 resonated up field at δ = 3.06 as a double doublet (J = 3.0, 16.6 Hz) and H-3′ resonated at δ = 2.82 as a double doublet (J = 3.0, 15.8 Hz) integrating for one proton each. IR spectrum revealed the presence of two carbonyl functional groups (1718 and 1655 cm^{-1}). The ^{13}C NMR spectrum revealed two carbonyl functionalities at δ = 164.79 and 205.76 ppm.



Scheme 5.

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Similarly, divinyl carbinol **3a** gave compound **10** (90%) as an exclusive product under the same set of reaction conditions (Scheme 5). The ^{1}H NMR and ^{13}C spectrum of compound **10** were similar to that of compound **9**, while compound **10**, $[a]_D$ = +33.92 (c = 0.2, $CHCl_3$); was having specific rotation value with opposite sign of **9**, $[a]_D$ = –38.87 (c = 0.55, $CHCl_3$), which clearly indicates that compounds **9** and **10** are enantiomeric to each other. Alternatively, the same transformation on substrates **2a** and **3a** could be affected by a moderate Lewis acid like $ZrCl_4$ in comparable time scales and yields. The reactions herein were cleaner. In this conversion an unprecedented Lewis acid mediated oxidation–reduction is taking place.

Though, at present the exact mechanism is not clear a plausible mechanism for formation of 3-deoxy sugar from divinyl carbinol system is depicted in Figure 1. Initially, Lewis acid coordinates with C5-OH (**A**), facilitating the quenching of C3 anion with H^+ and a simultaneous generation of oxonium ion **B**, whose extended stabilization leads to enolate **C** which on immediate stereospecific tautomerisation leads to **9** with the concomitant regeneration of Lewis acid. The stereospecificity may be explained due to the formation of a five-membered TS on the β-face (opposite to the a-acetonide moiety), prompting the unhindered reception of the incoming proton from the a-face. The distinguishing feature of the overall reaction is that the remotely placed acetonide moiety directs the magical transformation of a divinyl carbinol into a 3-deoxy sugar as an exclusive isomeric product.

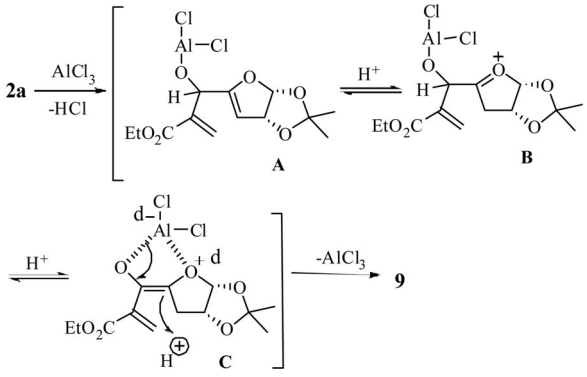

Figure 1. Plausible mechanism for the formation of 3-deoxy sugars.

The absolute stereochemistry at the newly created site (C4) in **9** and **10** was determined by a thorough NMR study. Thus, in compound **9** the NOE cross peak between H-4 and *pro*-'*R*'-Me, H-1 and *pro*-'*S*'-Me, support the assigned structure with the absolute stereochemistry at C-4 as '*S*'. Similarly, in compound **10**, the NOE cross peak between H-4 and *pro*-'*S*'-Me, H-1 and *pro*-'*R*'-Me, support the assigned structure with the absolute stereochemistry at C-4 as '*R*' (Figure 2).

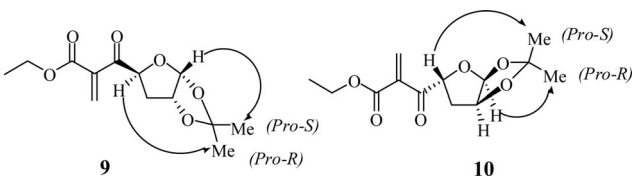

Figure 2. Schematic representation of NOEs.

Conclusions

It was demonstrated that an aldehyde carrying a properly positioned leaving group when subjected to the DABCO-catalyzed Baylis–Hillman reaction can be converted into divinyl carbinols, which upon exposure to Lewis acid afforded the corresponding 3-deoxy sugars as exclusive isomers in high yields. Also, these products would serve as valuable components in the synthesis of sugar-modified nucleosides.[10] Studies towards the applicability and limitations of this reaction and the complete understanding of the reaction mechanism are under investigation.

Experimental Section

General Experimental Procedure for Compound 1a, 2a and 3a: To an aldehyde (1 mmol) in dioxane/H_2O [(1:1), 5 mL], DABCO (1 mmol) and ethyl acrylate (3 mmol) were added and the reaction mixture stirred for 8 h at room temp. After complete conversion of the aldehyde, the reaction mixture was partitioned between ethyl acetate (3 × 15 mL) and water (1 × 25 mL) and the collected organic layers were washed with brine (25 mL), dried Na_2SO_4 and concentrated under reduced pressure to afford a residue, which was purified by column chromatography (silica gel 60–120 mesh, ethyl acetate:*n*-hexane, 2.5:7.5–3.0:7.0) to afford the adducts **1a**, **2a** and **3a** in 64, 80 and 86% yield.

General Experimental Procedure for Compound 9 and 10: To a stirred solution of divinyl carbinol **2a** and **3a** (1 mmol) in dry CH_2Cl_2 (10 mL), aluminum chloride (cat. amounts) was added and the reaction mixture stirred for 5 min at room temp. After completion of the reaction, the crude reaction mixture was concentrated, residue purified by column chromatography (silica gel 60–120 mesh, ethyl acetate:*n*-hexane 2.0–8.0) to afford **9** and **10** in 85% and 90% yield.

Ethyl 2-Hydroxy[(4*S*,5*R*)-4-hydroxy-5-methoxy-4,5-dihydro-2-furanyl]methylacrylate (1a): Methyl 2,3-*O*-isopropylidene-β-D-*ribo*-pentodialdo-1,4-furanose (**1**, 0.20 g, 1 mmol) in 1,4-dioxane/water [(1:1), 5 mL] was treated with ethyl acrylate **a** (0.32 mL, 3 mmol) in presence of DABCO (0.11 g, 1 mmol) at room temp. for 8 h. Then the reaction mixture was diluted with water (15 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layers was washed with brine (25 mL), dried (Na_2SO_4) and concentrated under reduced pressure to get a residue, which was purified by chromatography (silica gel 60–120 mesh, ethyl acetate:*n*-hexane, 8.5–1.5) to afford adduct **1a** (0.22 g, 64%) as a colorless syrup with 10% *de*. $[a]_D$ = –179.9 (c = 0.9, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 6.32 (s, 0.45 H, olefinic), 6.30 (s, 0.55 H, olefinic), 6.00 (s, 0.45 H, olefinic), 5.92 (s, 0.55 H, olefinic), 5.17 (d, J = 4.0 Hz, 0.55 H, olefinic), 5.14 (d, J = 4.0 Hz, 0.45 H, olefinic), 5.08 (m, 2 H, 1-H, and 5-H), 4.50 (br. s, 1 H, 2-H), 4.20 (m, 2 H, OCH_2), 3.9 (s, 1 H, OH), 3.43 (s, 1.33 H, OCH_3), 3.40 (s, 1.65 H, OCH_3), 1.3 (t, J = 6.68 Hz, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.09, 138.82, 127.07, 112.58, 100.37, 99.98, 78.48, 66.78, 61.11, 56.01, 55.89 ppm. IR (neat): $\tilde{\nu}$ = 3430, 2934, 1717

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cm^{-1}. FABMS: *m*/*z*: 245 [M^+ + 1]. $C_{11}H_{16}O_6$ (244.24): calcd. C 54.09, H 6.60; found C 54.05, H 6.54.

Ethyl 2-{[(3a*R*,6a*R*)-2,2-Dimethyl-3a,6a-dihydrofuro[2,3-*d*][1,3]-dioxol-5-yl](hydroxy)methyl}acrylate (2a): (3a*R*,5*S*,6*S*,6a*R*)-5-Formyl-2,2-dimethylperhydrofuro[2,3-*d*][1,3]dioxol-6-yl 4-methyl-1-benzenesulfonate (**2**, 0.20 g, 1 mmol) in 1,4-dioxane/water [(1:1), 5 mL] was treated with ethyl acrylate **a** (0.19 mL, 3 mmol) in presence of DABCO (0.65 g, 1 mmol) at room temp. for 8 h. The reaction mixture was worked up and purified as described for **1a** to give **2a** (0.12 g, 80%) as pale yellow syrup with 36% *de*. $[\alpha]_D$ = +113.44 (*c* = 0.25, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 6.34 (s, 1 H, olefinic), 6.10 (d, *J* = 5.2 Hz, 1 H, 1-H), 5.94 (d, *J* = 1.5 Hz, 1 H, olefinic), 5.30–5.22 (m, 1 H, 3-H), 5.17–5.13 (m, 1 H, 2-H), 4.95 (br. d, *J* = 7.4 Hz, 1 H, 5-H), 4.30–4.20 (m, 2 H, CH_2), 3.32 (d, *J* = 1.42 Hz, 0.68 H, OH), 3.32 (d, *J* = 1.42 Hz, 0.32 H, OH), 1.38 (s, 6 H, 2 × CH_3), 1.35–1.25 (m, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.73 160.78, 138.09, 127.29, 112.11, 106.33, 83.40, 67.41, 61.01, 27.94, 27.84, 27.71, 13.95 ppm. IR (neat): $\tilde{\nu}$ = 3439, 2985, 2934, 1719, 1633 cm^{-1}. ES$^+$MS: *m*/*z*: 271 [M^+ + 1]. $C_{13}H_{18}O_6$ (270.28): calcd. C 57.77, H 6.71; found C 57.73, H 6.67.

Ethyl 2-{[(3a*S*,6a*S*)-2,2-Dimethyl-3a,6a-dihydrofuro[2,3-*d*][1,3]dioxol-5-yl](hydroxy)methyl}acrylate (3a): (3a*S*,5*S*,6*S*,6a*S*)-5-Formyl-2,2-dimethylperhydrofuro[2,3-*d*][1,3]dioxol-6-yl 4-methyl-1-benzenesulfonate (**3**, 0.20 g, 1 mmol) in 1,4-dioxane/water [(1:1), 5 mL] was treated with ethyl acrylate **a** (0.19 mL, 3 mmol) in presence of DABCO (0.65 g, 1 mmol) at room temp. for 8 h. The reaction mixture was worked up and purified as described for **1a** to give **3a** (0.13 g, 86%) as pale yellow syrup with 32% *de*. $[\alpha]_D$ = –111.8 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 6.33 (s, 1 H, olefinic), 6.05 (d, *J* = 5.3 Hz, 1 H, 1-H), 5.93 (s, 1 H, olefinic), 5.29–5.23 (m, 1 H, 3-H), 5.17–5.13 (m, 1 H, 2-H), 4.95 (m, 1 H, 5-H), 4.30–4.18 (m, 2 H, CH_2), 3.21 (dd, *J* = 3.08, 8.31 Hz, 0.66 H, OH), 3.14 (dd, *J* = 3.08, 8.31 Hz, 0.34 H, OH), 1.40 (s, 6 H, 2 × CH_3), 1.34–1.24 (m, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.77, 160.57, 138.14, 127.37, 112.13, 106.37, 99.00, 83.45, 67.53, 61.03, 26.04 (2 C), 13.99 ppm. IR (neat): $\tilde{\nu}$ = 3438, 2983, 2934, 1718 cm^{-1}. ES$^+$MS: *m*/*z*: 271 [M^+ + 1]. $C_{13}H_{18}O_6$ (270.28): calcd. C 57.77, H 6.71; found C 57.70, H 6.65.

4-Hydroxy-5-methoxy-4,5-dihydrofuran-2-carbaldehyde (6): Methyl 2,3-*O*-isopropylidene-β-D-*ribo*-pentodialdo-1,4-furanose (**1**, 0.1 g, 0.49 mmol) in dioxane/H_2O [(1:1), 2 mL], DABCO (0.06 g, 0.49 mmol) was added and the reaction mixture stirred for 2 h at room temp. After complete conversion of the aldehyde, the reaction mixture was partitioned between ethyl acetate (3 × 15 mL) and water (1 × 20 mL) and the collected organic layers were washed with brine (20 mL), dried (Na_2SO_4) and concentrated under reduced pressure to afford a residue, which was purified by column chromatography (silica gel 60–120 mesh, ethyl acetate:*n*-hexane, 2.5:7.5–3.0:7.0) to afford aldehyde **6** (0.044 g, 63%). ^{1}H NMR (300 MHz): δ = 9.50 (s, 1 H, CHO), 6.06 (d, *J* = 2.8 Hz, 1 H, CH), 5.07 (d, *J* = 5.6 Hz, 1 H, CH), 4.63 (d, *J* = 5.6 Hz, 1 H, CH), 3.53 (s, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz): δ = 183.3, 156.9, 118.5, 113.4, 78.2, 56.8 ppm. IR (neat): $\tilde{\nu}$ = 3390, 2990, 1710, 1620, 1190 cm^{-1}. EI-MS: 145 [M^+ + 1]. $C_6H_8O_4$ (144.13): calcd. C 50.00, H 5.59; found C 50.02, H 5.60.

(2,2-Dimethyl-3a,6a-dihydrofuro[2,3-*d*][1,3]dioxol-5-yl)methanol (7): (3a*R*,5*S*,6*S*,6aR)-5-Formyl-2,2dimethylperhydrofuro[2,3-*d*][1,3]dioxol-6-yl 4-methyl-1-benzenesulfonate(**2**, 0.1 g, 0.29 mmol) in dioxane/H_2O [(1:1), 5 mL], DABCO (0.033 g, 0.29 mmol) was added and the reaction mixture stirred for 2 h at room temp. The reaction mixture was worked up as described for **6** to afford a residue, which was directly treated with $NaBH_4$ (0.011 g, 0.29 mmol) in MeOH at 0 °C to room temp. for 1 h. After completion of the reaction MeOH was removed under reduced pressure and obtained residue was partitioned between ethyl acetate (3 × 15 mL) and water (1 × 20 mL) and the collected organic layers were washed with brine (20 mL), dried (Na_2SO_4) and concentrated under reduced pressure to afford a residue, which was purified by column chromatography (silica gel 60–120 mesh, ethyl acetate:*n*-hexane, 2.5:7.5–3.0:7.0) to afford alcohol **7** (0.035 g, 70%, over 2 steps). $[\alpha]_D$ = +55.6 (*c* = 0.5, $CHCl_3$). ^{1}HNMR (300 MHz): δ = 6.02 (d, *J* = 5.2 Hz, 1 H, CH), 5.26 (d, *J* = 6.7 Hz, 1 H, CH), 5.12 (m, 1 H, CH), 4.12 (s, 2 H, CH_2), 1.43 (s, 3 H, CH_3), 1.41 (s, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz): δ = 113.0, 106.0, 105.2, 80.1, 66.6, 40.5, 27.5, 26.3 ppm. IR (neat): $\tilde{\nu}$ = 3400, 3020, 1610, 1230 cm^{-1}. EI-MS: 173 [M^+ + 1]. $C_8H_{12}O_4$ (172.18): calcd. C 55.81, H 7.02; found C 55.84, H 7.04.

(2,2-Dimethyl-3a,6a-dihydrofuro[2,3-*d*][1,3]dioxol-5-yl)methanol (8): (3a*S*,5*S*,6*S*,6a*S*)-5-Formyl-2,2-dimethylperhydrofuro[2,3-*d*][1,3]dioxol-6-yl 4-methyl-1-benzenesulfonate (**3**, 0.1 g, 0.29 mmol) in dioxane/H_2O [(1:1), 5 mL], DABCO (0.033 g, 0.29 mmol) was added and the reaction mixture stirred for 2 h at room temp. The reaction mixture was worked up as described for **6** to afford a residue, which was directly treated with $NaBH_4$ (0.011 g, 0.29 mmol) in MeOH at 0 °C to room temp. for 1 h. The reaction mixture was worked up and purified as described for **7** to give **8** (0.035 g, 70% over 2 steps). $[\alpha]_D$ = –54.4 (*c* = 0.5, $CHCl_3$). ^{1}HNMR (300 MHz): δ = 6.02 (d, *J* = 5.2 Hz, 1 H, CH), 5.26 (d, *J* = 6.7 Hz, 1 H, CH), 5.12 (m, 1 H, CH), 4.12 (s, 2 H, CH_2), 1.43 (s, 3 H, CH_3), 1.41 (s, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz): δ = 113.0, 106.0, 105.2, 80.1, 66.6, 40.5, 27.5, 26.3 ppm. IR (neat): $\tilde{\nu}$ = 3400, 3020, 1610, 1230 cm^{-1}. EI-MS: 173 [M^+ + 1]. $C_8H_{12}O_4$ (172.07): calcd. C 55.81, H 7.02; found C 55.84, H 7.04.

Ethyl 2-[(3a*R*,6a*R*)-2,2-Dimethyl-3a,6a-dihydrofuro[2,3-*d*][1,3]dioxol-5-yl]carbonylacrylate (9): To a stirred solution of ethyl 2-{[(3a*R*,6a*R*)-2,2-dimethyl-3a,6a-dihydrofuro[2,3-*d*][1,3]dioxol-5-yl](hydroxy)methyl}acrylate (**2a**, 0.10 g, 1 mmol) in dry CH_2Cl_2, aluminum chloride (cat. amounts) was added, stirred at room temp. for 5 min. After completion of the reaction, the crude reaction mixture was concentrated, residue purified by column chromatography (silica gel 60–120 mesh, ethyl acetate:*n*-hexane 2.0–8.0) to afford adduct **9** (0.08, 85%) as a colorless syrup. $[\alpha]_D$ = –38.87 (*c* = 0.55, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ = 6.42 (s, 1 H, olefinic), 5.92 (s, 1 H, olefinic), 5.72 (d, *J* = 5.3 Hz, 1 H, 1-H), 4.77 (br. s, 1 H, 4-H), 4.74–4.70 (m, 1 H, 2-H), 4.32–4.28 (q, *J* = 6.8 Hz, 2 H, CH_2), 3.06 (dd, *J* = 3.0, 16.6 Hz, 1 H, 3-H), 2.82 (dd, *J* = 3.0, 16.6 Hz, 1 H, 3′-H), 1.57 (s, 3 H, CH_3), 1.38 (s, 3 H, CH_3), 1.31 (t, *J* = 6.8 Hz, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 205.76, 164.79, 136.38, 130.69, 109.31, 97.28, 76.20, 73.26, 61.37, 38.92, 26.07, 25.84, 14.03 ppm. IR (neat): $\tilde{\nu}$ = 3501, 2986, 2929, 1718, 1655 cm^{-1}. ES$^+$MS: *m*/*z*: 271 [M^+ + 1]. $C_{13}H_{18}O_6$ (270.28): calcd. C 57.77, H 6.71; found C 57.79, H 6.58.

Ethyl 2-[(3a*S*,6a*S*)-2,2-Dimethyl-3a,6a-dihydrofuro[2,3-*d*][1,3]dioxol-5-yl]carbonylacrylate (10): To a stirred solution of ethyl 2-{[(3a*S*,6a*S*)-2,2-dimethyl-3a,6a-dihydrofuro[2,3-*d*][1,3]dioxol-5-yl]-(hydroxy)methyl}acrylate (**3a**, 0.10 g, 1 mmol) in dry CH_2Cl_2, aluminum chloride was added, stirred at room temp. for 5 min. The reaction mixture was worked up and purified as described for **9** to give **10** in (0.09, 95%) as a colorless syrup. $[\alpha]_D$ = +33.92 (*c* = 0.2, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ = 6.45 (s, 1 H, olefinic), 6.95 (s, 1 H, olefinic), 5.73 (d, *J* = 5.3 Hz, 1 H, 1-H), 4.76 (br. s, 1 H, 4-H), 4.76–4.71 (m, 1 H, 2-H), 4.22 (q, *J* = 7.5 Hz, 2 H, CH_2), 3.07 (dd, *J* = 3.0, 16.6 Hz, 1 H, 3-H), 2.84 (dd, *J* = 3.0,

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16.6 Hz, 1 H, 3′-H), 1.57 (s, 3 H, CH_3), 1.38 (s, 3 H, CH_3), 1.30 (t, J = 7.5 Hz, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 205.97, 164.79, 136.24, 130.77, 109.30, 97.22, 77.20, 73.20, 61.23, 38.89, 26.07, 25.84, 14.04 ppm. IR (neat): $\tilde{\nu}$ = 3502, 2986, 2929, 1718, 1655 cm^{-1}. ES^+MS: *m*/*z*: 271 [M^+ + 1]. $C_{13}H_{18}O_6$ (270.28): calcd. C 57.77, H 6.71; found C 57.72, H 6.66.

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