## A Novel Prins Bicyclization Strategy for the Synthesis of Sugar Annulated Furopyran Scaffolds

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**Abstract:** A tandem Prins bicyclization of sugar-derived homoallylic diols with aldehydes has been accomplished using 10 mol% of  $In(OTf)_3$  and 20 mol% of TsOH at ambient temperature to produce a novel series of sugar-annulated furopyran derivatives in good yields with high selectivity. This is the first report on Prins bicyclization of homoallylic diols derived from sugars. The cooperative catalysis between  $In(OTf)_3$  and TsOH provides high conversions and enhanced reaction rates.

**Key words:** Prins bicyclization, D-glucose, sugar-annulated heterocycles, metal triflate, cooperative catalysis

The Prins cyclization is one of the most elegant methods for the construction of tetrahydropyran derivatives with a high degree of stereoselectivity<sup>1</sup> and has been utilized for the synthesis of several natural products.<sup>2</sup> Typically, acid catalysts are known to catalyze the Prins cyclization to produce a large number of tetrahydropyran derivatives under mild conditions.<sup>3,4</sup> Recently, a cascade of Prins cyclization has been reported to generate a wide range of tetrahydropyran derivatives.<sup>5,6</sup> However, to the best of our knowledge, there are no reports on Prins bicyclization between an aldehyde and homoallylic diol derived from sugars. These scaffolds are very useful for biological screening against various cancer cell lines.

In continuation of our interest on Prins cyclization,<sup>7</sup> we herein report a novel method for the synthesis of sugarannulated furopyran derivatives through Prins bicyclization between sugar-based homoallylic diols and aldehydes. In a model reaction, we first attempted the crosscoupling of sugar homoallylic diol **1a** with benzaldehyde (**2**) in the presence of 4 Å MS using 10 mol% In(OTf)<sub>3</sub> and 20 mol% PTSA in dichloroethane. Interestingly, the reaction proceeded smoothly at room temperature and the corresponding product **3a** was obtained in 80% yield with *cis* selectivity (entry 1, Table 1, and Scheme 1).

Inspired by the above result, we extended this method to various aldehydes such as *m*-tolualdehyde, *m*-methoxybenzaldehyde, *p*-methoxybenzaldehyde, *p*-fluorobenzaldehyde, *p*-chlorobenzaldehyde and *p*-bromobenzaldehyde. Interestingly, several aromatic aldehydes participated effectively in this reaction (entries 1–9, Table 1). Remarkably, a sterically hindered 2-naphthaldehyde and 1-pyrenecarboxaldehyde also gave the desired products in

*SYNLETT* 2013, 24, 1263–1268 Advanced online publication: 08.05.2013 DOI: 10.1055/s-0033-1338708; Art ID: ST-2013-D0146-L © Georg Thieme Verlag Stuttgart · New York excellent yields (entries 8 and 9, Table 1). The substituent on aromatic ring showed some effect on the conversion. It was observed that electron-rich aromatic aldehydes gave the products in relatively lower yields than unsubstituted or halogenated aryl aldehydes (Table 1). The structure and stereochemistry of **3c** were confirmed by NOE and X-ray experiments (see Supporting Information).<sup>8</sup>



Scheme 1 Prins bicyclization of 1a with benzaldehyde (2)

The geometry of the olefin controls the stereoselectivity of the reaction. It is known that *cis*-olefin gives the *cis*fused product exclusively. The use of molecular sieves is essential to avoid the cleavage of sugar acetonide. The combination of In(OTf)<sub>3</sub> and TsOH (1:2) works more effectively than either In(OTf)<sub>3</sub> or TsOH alone. The high catalytic activity of the above reagent system may be explained through a cooperative catalysis between In(OTf)<sub>3</sub> and TsOH.9 Other Brønsted acids such as TFA, TfOH, CSA as well as Lewis acids such as Sc(OTf)<sub>3</sub>, Yb(OTf)<sub>3</sub>, In(OTf)<sub>3</sub> were screened for this conversion. Among them, the combination of In(OTf)<sub>3</sub> and TsOH (1:3) afforded the best results in Prins bicyclization (Table 1). However, in the absence of catalyst, no reaction was observed under similar conditions. Next, we examined the effect of various solvents such as tetrahydrofuran, 1,2-dimethoxyethane and 1,2-dichloroethane. Among them, 1,2dichloroethane gave the best results. Mechanistically, the reaction is expected to proceed through oxocarbenium ion which is formed in situ from hemiacetal, likely after activation of the aldehyde with PTSA. Subsequent attack of the olefin on oxocarbenium generates the carbocation which is simultaneously trapped with a tethered secondary hydroxyl group leading to the formation of sugarannulated furopyran as depicted in Scheme 2.

 Table 1
 Prins Bicyclization of Sugar-Derived Homoallylic Diols with Aldehydes

Entry	Homoallylic diol	Aldehy	de 2	Product	<b>3</b> <sup>a</sup>	Time (h)	Yield (%) <sup>b</sup>
1	1a HO HO HO	2a	СНО	3a		6.0	80
2	1a	2b	MeCHO	3b	H H H	6.1	68
3	1a	2c	MeO	3c	O OMe	5.8	78
4	1a	2d	MeO	3d	OMe H H O H	6.2	75
5	1a	2e	F CHO	3e	F H H H	5.5	80
6	1a	2f	СІСНО	3f		6.0	82

Entry	Homoallylic diol	Aldehyde 2		Produc	Product <b>3</b> <sup>a</sup>		Time (h) Yield (%) <sup>h</sup>	
7	1a	2g	Br	3g	Br H H O H	5.0	85	
8	1a	2h	СНО	3h		5.2	82	
9	1a	2i	СНО	3i		5.0	87	
10	1b HO OH	2j	F CHO	3j		6.0	79	

 Table 1
 Prins Bicyclization of Sugar-Derived Homoallylic Diols with Aldehydes (continued)

<sup>a</sup> All products were characterized by NMR, IR and mass spectroscopy. <sup>b</sup> Yield refers to pure products after chromatography.

In order to demonstrate the scope of this method, the reaction was also performed with acetonide-protected sugar homoallylic diol **1b**. The cross-coupling of **1b** with 2fluorobenzaldehyde proceeded well under similar conditions to afford the desired product **3j** in 78% yield with *cis* selectivity (entry 10, Table 1).

The present method is simple and convenient and also provides the desired products in good to excellent yields with high stereoselectivity. All the products were characterized and confirmed by NMR, IR and mass spectrometry. The scope and generality of this process is illustrated with respect to various aldehydes and the results are presented in Table 1.<sup>10</sup>

In summary, we have demonstrated a novel approach for the synthesis of sugar-annulated furopyran derivatives through Prins bicyclization using a combination of  $In(OTf)_3$  and PTSA. This method provides a direct access to the synthesis of a wide range of sugar-fused furopyrans in a single-step process. This approach is highly stereoselective, affording the *cis*-fused tricyclic ethers in a singlestep process.

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**Supporting Information** for this article is available online at http://www.thieme-connect.com/ejournals/toc/synlett.



Scheme 2 A plausible reaction pathway

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- (10) General Procedure: To a stirred solution of homoallylic diol (1a; 100 mg, 0.37 mmol) in the presence of 4 Å MS were added aldehyde (2, 0.44 mmol), followed by  $In(OTf)_3$  (10 mol%) and TsOH (20 mol%) in anhyd DCE (5 mL) at 0 °C. The resulting mixture was stirred at r.t. under a nitrogen atmosphere for the specified time (Table ). After completion of the reaction as indicated by TLC, the mixture was quenched with sat. aq NaHCO<sub>3</sub> solution (0.5 mL) and extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 × 10 mL). The combined organic phases were washed with brine (3 × 2 mL), dried over anhyd Na<sub>2</sub>SO<sub>4</sub> and concentrated in vacuo. The crude product was purified by silica gel column chromatography (60–120 mesh) using EtOAc–hexane (3:7) as eluent to afford the pure product **3**.

(3a*R*,4a*R*,4b*S*,5*R*,8a*S*,9a*S*,9b*R*)-5-Phenyloctahydro-3a*H*-spiro([1,3]dioxolo[4'',5'':4',5']furo[2',3':4,5]furo-[3,2-c]pyran-2,1'-cyclohexane) (3a): viscous liquid;  $[\alpha]_D^{25}$ +16.9 (c 0.5, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.47– 1.65 (m, 10 H), 1.85–1.94 (m, 2 H), 2.39–2.46 (m, 1 H), 3.45–3.53 (m, 1 H), 4.16–4.21 (m, 1 H), 4.35 (d, *J* = 3.1 Hz, 1 H), 4.39 (t, *J* = 3.1 Hz, 1 H), 4.45 (dd, *J* = 7.9, 9.5 Hz, 1 H), 4.55 (d, *J* = 3.1 Hz, 1 H), 4.71 (d, *J* = 4.7 Hz, 1 H), 6.03 (d, *J* = 3.9 Hz, 2 H), 7.25–7.31 (m, 1 H), 7.36 (t, *J* = 7.1 Hz, 2 H), 7.51 (d, *J* = 7.9 Hz, 1 H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$ = 23.5, 23.7, 24.8, 31.9, 31.4, 36.6, 36.1, 47.6, 65.5, 77.2, 78.3, 82.8, 83.5, 87.6, 107.0, 126.3, 127.5, 128.3. IR (neat): 3430, 2927, 2854, 1731, 1074, 804, 701 cm<sup>-1</sup>. ESI–MS: *m/z* = 359. HRMS (ESI): *m/z* [M + Na]<sup>+</sup> calcd for C<sub>21</sub>H<sub>26</sub>O<sub>5</sub>: 381.1672; found: 381.1676.

(3a*R*,4a*R*,4b*S*,5*R*,8a*S*,9a*S*,9b*R*)-5-(*m*-Tolyl)octahydro-3a*H*-spiro([1,3]dioxolo[4",5":4',5']furo [2',3':4,5]furo-[3,2-*c*]pyran-2,1'-cyclohexane) (3b): viscous liquid;  $[\alpha]_D^{25}$ +35.5 (*c* 0.25, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.40–1.70 (m, 10 H), 1.84–1.95 (m, 2 H), 2.34–2.38 (s, 3 H), 2.39–2.46 (m, 1 H), 3.43–3.46 (m, 1 H), 4.15–4.23 (m, 1 H), 4.36 (d, *J* = 3.0 Hz, 1 H), 4.41–4.49 (m, 2 H), 4.57 (d, *J* = 3.7 Hz, 1 H), 4.68 (d, *J* = 4.5 Hz, 1 H), 6.05 (d, *J* = 3.7 Hz, 1 H), 7.10 (d, *J* = 6.7 Hz, 1 H), 7.25–7.43 (m, 3 H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 21.4, 23.6, 23.8, 24.8, 31.5, 31.9, 36.3, 36.6, 47.6, 65.6, 77.2, 78.4, 82.8, 83.5, 87.5, 107.0, 123.4, 127.1, 128.1, 128.2. IR (neat): 3434, 2929, 2854, 1734, 1454, 1109, 772 cm<sup>-1</sup>. ESI–MS: *m/z* = 373 [M + H]<sup>+</sup>. HRMS (ESI): *m/z* [M + Na]<sup>+</sup> calcd for C<sub>22</sub>H<sub>28</sub>O<sub>5</sub>: 395.1829; found: 395.1831.

(3a*R*,4a*R*,4b*S*,5*R*,8a*S*,9a*S*,9b*R*)-5-Phenyloctahydro-3a*H*-spiro([1,3]dioxolo[4'',5'':4',5']furo[2',3':4,5]furo-[3,2-*c*]pyran-2,1'-cyclohexane) (3c): viscous liquid;  $[\alpha]_D^{25}$ +22 (*c* 0.3, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.30– 1.61 (m, 10 H), 1.88–1.91 (m, 2 H), 2.40 (m, 1 H), 3.46–3.52 (m, 1 H), 3.84 (s, 3 H), 4.15–4.21 (m, 1 H), 4.35 (d, *J* = 3.0 Hz, 1 H), 4.40–4.46 (m, 2 H), 4.58 (d, *J* = 4.0 Hz, 1 H), 4.68 (d, *J* = 4.0 Hz, 1 H), 6.04 (d, *J* = 4.0 Hz, 1 H), 6.85 (dd, *J* = 3.0, 9.0 Hz, 1 H), 7.00 (d, J = 8.0 Hz, 1 H), 7.23–7.28 (m, 2 H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 23.6, 23.8, 24.8, 36.2, 36.7, 47.5, 55.3, 65.6, 77.2, 78.5, 82.9, 83.5, 87.4, 106.9, 111.2, 112.2, 114.5, 118.8, 129.1, 141.6. IR (neat): 3455, 2930, 2855, 1729, 1603, 1107, 772 cm<sup>-1</sup>. ESI–MS: <math>m/z = 389$  [M + H]<sup>+</sup>. HRMS (ESI): m/z [M + Na]<sup>+</sup> calcd for C<sub>22</sub>H<sub>28</sub>O<sub>6</sub>: 411.1778; found: 411.1767.

(3a*R*,4a*R*,4b*S*,5*R*,8a*S*,9a*S*,9b*R*)-5-(4-Methoxyphenyl)octahydro-3a*H*-spiro([1,3]dioxolo[4'',5'':4',5']-furo[2',3':4,5]furo[3,2-c]pyran-2,1'-cyclohexane) (3d): viscous liquid;  $[\alpha]_D^{25}$ +11 (*c* 0.25, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.45–1.65 (m, 10 H), 1.82–1.91 (m, 2 H), 2.35–2.41 (m, 1 H), 3.42–3.52 (m, 1 H), 3.81 (s, 3 H), 4.13–4.20 (m, 1 H), 4.35 (d, *J* = 2.9 Hz, 1 H), 4.39–4.44 (m, 2 H), 4.57 (d, *J* = 3.9 Hz, 1 H), 4.66 (d, *J* = 3.9 Hz, 1 H), 6.04 (d, *J* = 3.9 Hz, 1 H), 6.90 (d, *J* = 7.7 Hz, 2 H), 7.45 (d, *J* = 8.7 Hz, 2 H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 23.6, 23.8, 24.8, 31.9, 36.2, 47.9, 55.2, 65.6, 78.1, 82.9, 83.6, 87.6, 107.0, 112.2, 113.6, 127.7. IR (neat): 2924, 2853, 1735, 1458, 1106, 1070 cm<sup>-1</sup>. ESI–MS: *m/z* = 406 [M + NH<sub>4</sub>]<sup>+</sup>. HRMS (ESI): *m/z* [M + Na]<sup>+</sup> calcd for C<sub>22</sub>H<sub>28</sub>O<sub>6</sub>: 411.1778; found: 411.1767.

(3a*R*,4a*R*,4b*S*,5*R*,8a*S*,9a*S*,9b*R*)-5-(4-Fluorophenyl)octahydro-3a*H*-spiro([1,3]dioxolo[4",5":4',5']-furo[2',3':4,5]furo[3,2-*c*]pyran-2,1'-cyclohexane) (3e): semi-solid;  $[\alpha]_D^{25}$ +17 (*c* 0.5, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.45–1.65 (m, 10 H), 1.82–1.93 (m, 2 H), 2.36–2.42 (m, 1 H), 3.44–3.51 (m, 1 H), 4.14–4.20 (m, 1 H), 4.34–4.37 (s, 2 H), 4.43 (dd, *J* = 7.7, 11.0 Hz, 1 H), 4.57 (d, *J* = 3.3 Hz, 1 H), 4.69 (d, *J* = 4.4 Hz, 1 H), 6.02 (d, *J* = 3.3 Hz, 1 H), 7.05 (t, *J* = 8.8 Hz, 2 H), 7.50 (dd, *J* = 3.3, 5.5 Hz, 2 H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 23.6, 23.8, 24.8, 31.4, 36.1, 36.6, 47.7, 65.5, 77.7, 82.7, 83.6, 87.5, 107.0, 112.3, 115.0, 115.1, 128.0, 128.1, 135.9. IR (neat): 3460, 2928, 2854, 1728, 1602, 1102, 800 cm<sup>-1</sup>. ESI–MS: *m*/*z* = 377 [M + H]<sup>+</sup>. HRMS (ESI): *m*/*z* [M + Na]<sup>+</sup> calcd for C<sub>21</sub>H<sub>25</sub>FO<sub>5</sub>: 399.1578; found: 399.1574.

(3aR,4aR,4bS,5R,8aS,9aS,9bR)-5-(4Chlorophenyl)octahydro-3aH-spiro([1,3]dioxolo[4",5":4',5']furo[2',3':4,5]furo[3,2-c]pyran-2,1'-cyclohexane) (3f): semi-solid;  $[\alpha]_D^{25}$  +19 (c 0.5, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz,  $CDCl_3$ ):  $\delta = 1.46-1.60 (m, 10 H), 1.86-1.94 (m, 2 H), 2.37-$ 2.45 (m, 1 H), 3.43–3.53 (m, 1 H), 4.13–4.21 (m, 1 H), 4.34– 4.38 (m, 2 H), 4.45 (dd, J = 7.5, 10.5 Hz, 1 H), 4.58 (d, J = 3.7 Hz, 1 H), 4.70 (d, J = 4.5 Hz, 1 H), 6.03 (d, J = 3.7 Hz, 1 H), 7.32–7.38 (m, 2 H), 7.42–7.48 (m, 2 H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ = 23.6, 23.8, 24.9, 31.4, 36.1, 36.6, 47.5, 65.5, 77.5, 82.7, 83.6, 87.6, 107.0, 112.3, 127.8, 128.4, 138.7. IR (neat): 3782, 3682, 2930, 2855, 1732, 1105, 823  $cm^{-1}$ . ESI-MS:  $m/z = 393 [M + H]^+$ . HRMS (ESI):  $m/z [M + H]^+$ Na]<sup>+</sup> calcd for C<sub>21</sub>H<sub>25</sub>ClO<sub>5</sub>: 415.1282; found: 415.1275. (3aR,4aR,4bS,5R,8aS,9aS,9bR)-5-(4-Bromophenyl)octahydro-3aH-spiro([1,3]dioxolo[4",5":4',5']furo[2',3':4,5]furo[3,2-c]pyran-2,1'-cyclohexane) (3g): solid; mp 146–148 °C; [α]<sub>D</sub><sup>25</sup> +23.8 (*c* 0.25, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta = 1.42 - 1.66$  (m, 10 H), 1.82-1.92 (m, 2 H), 2.35–2.45 (m, 1 H), 3.42–3.54 (m, 1 H), 4.12– 4.21 (m, 1 H), 4.33-4.38 (m, 2 H), 4.45 (dd, J = 7.5, 10.5 Hz)1 H), 4.57 (d, J=3.8 Hz, 1 H), 4.68 (d, J=4.5 Hz, 1 H), 6.02 (d, J = 3.8 Hz, 1 H), 7.39 (d, J = 8.3 Hz, 2 H), 7.50 (d, J = 9.0 Hz, 2 H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 23.5, 23.7, 24.8, 31.3, 36.0, 36.6, 47.3, 65.4, 76.8, 77.5, 82.7, 83.5, 87.6, 106.9, 112.3, 121.3, 128.0, 131.3, 139.1. IR (neat): 3451, 2933, 2856, 1631, 1108 cm<sup>-1</sup>. ESI–MS: m/z = 454 [M +

 $NH_4$ ]<sup>+</sup>. HRMS (ESI): *m*/*z* [M + Na]<sup>+</sup> calcd for C<sub>21</sub>H<sub>25</sub>BrO<sub>5</sub>: 459.0777; found: 459.0777.<sup>+</sup>

(3aR,4aR,4bS,5R,8aS,9aS,9bR)-5-(Naphthalen-2yl)octahydro-3aH-spiro([1,3]dioxolo[4",5":4',5']furo[2',3':4,5]furo[3,2-c]pyran-2,1'-cyclohexane) (3h): viscous liquid;  $[\alpha]_D^{25}$  +9 (*c* 0.25, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta = 1.40 - 1.67$  (m, 10 H), 1.87 - 1.99 (m, 2 H), 2.52-2.58 (m, 1 H), 3.53-3.60 (m, 1 H), 4.22-4.29 (m, 1 H), 4.37 (d, J = 3.0 Hz, 1 H), 4.40 (t, J = 3.0 Hz, 1 H), 4.50 (q, J)= 9.0 Hz, 1 H), 4.58 (d, J = 4.0 Hz, 1 H), 4.90 (d, J = 4.0 Hz, 1 H), 6.02 (d, J = 3.0 Hz, 1 H), 7.46–7.51 (m, 2 H), 7.68 (d, J = 7.0 Hz, 1 H), 7.82–7.91 (m, 3 H), 7.97 (s, 1 H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ = 23.5, 23.7, 24.8, 31.5, 36.1, 36.5, 47.6, 65.6, 77.2, 78.3, 82.8, 83.5, 87.6, 107.0, 113.7, 124.3, 125.1, 125.7, 125.9, 127.6, 128.1, 127.6. IR (neat): 2924, 2852, 1736, 1461, 1219, 772 cm<sup>-1</sup>. ESI-MS: m/z = 409 [M+ H]<sup>+</sup>. HRMS (ESI): m/z [M + Na]<sup>+</sup> calcd for C<sub>25</sub>H<sub>28</sub>O<sub>5</sub>: 431.1829; found: 431.1822

(3a*R*,4a*R*,4b*S*,5*R*,8a*S*,9a*S*,9b*R*)-5-(4,5*a*1-Dihydropyren1yl)octahydro-3a*H*-spiro([1,3]dioxolo-

[4",5":4',5']furo[2',3':4,5]furo[3,2-c]pyran-2,1'**cyclohexane) (3i)**: semi-solid;  $[\alpha]_D^{25} + \bar{1}94$  (*c* 0.25, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 1.30-1.61$  (m, 10 H), 1.98– 2.09 (m, 2 H), 2.76–2.86 (m, 1 H), 3.60–3.80 (m, 1 H), 4.03 (t, J = 3.0 Hz, 1 H), 4.26 (d, J = 3.0 Hz, 1 H), 4.31-4.40 (m, J = 3.0 Hz, 1 H)1 H), 4.56 (d, J = 3.7 Hz, 1 H), 4.80 (dd, J = 8.3, 9.0 Hz, 1 H), 5.82 (d, J = 4.5 Hz, 1 H), 6.04 (d, J = 3.7 Hz, 2 H), 7.95-8.04 (m, 1 H), 8.07 (d, J = 3.7 Hz, 1 H), 8.11 (d, J = 1.5 Hz, 2 H), 8.18 (dd, J = 3.0, 4.5 Hz, 2 H), 8.29 (d, J = 8.3 Hz, 1 H), 8.60 (d, J = 7.5 Hz, 1 H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$ = 23.5, 23.6, 24.7, 36.0, 36.6, 46.9, 65.9, 74.6, 76.9, 82.9, 83.4, 87.5, 106.9, 112.2, 121.6, 124.4, 124.9, 125.2, 125.3, 125.4, 125.7, 126.1, 126.9, 127.6, 127.7, 130.3, 130.4, 131.2, 133.6. IR (neat): 3445, 2929, 2854, 1729, 1366, 1106, 846 cm<sup>-1</sup>. ESI–MS:  $m/z = 505 [M + Na]^+$ . HRMS (ESI): m/z $[M + Na]^+$  calcd for  $C_{31}H_{30}O_5$ : 505.1985; found: 505.1982. (3aR,4aR,5R,9aS,9bR)-5-(2-Fluorophenyl)-2,2dimethyloctahydro-3aH-([1,3]dioxolo[4",5":4',5']furo-[2',3':4,5]furo[3,2-c]pyran) (3j):  $[\alpha]_D^{25}$  +50.2 (c 0.50, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta = 1.30-1.75$  (m, 6 H), 1.80-1.98 (m, 2 H), 2.27-2.38 (m, 2 H), 3.47-3.58 (m, 1 H), 4.13–4.25 (m, 1 H), 4.35 (d, J=10.8 Hz, 1 H), 4.42–4.50 (m, 1 H), 4.58 (d, J = 2.8 Hz, 1 H), 5.07 (d, J = 2.7 Hz, 1 H), 6.02 (d, J = 3.0 Hz, 1 H), 6.93–7.09 (m, 2 H), 7.18–7.41 (m, 1 H), 7.76–7.86 (m, 1 H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta =$ 22.7, 26.6, 26.9, 45.7, 62.1, 65.5, 71.4, 83.2, 83.9, 87.4, 107.4, 111.5, 114.3, 114.5, 123.9, 124.4, 124.5, 127.2, 127.3, 128.7, 128.8, 157.9, 159.8. IR (neat): 2925, 2854, 1742, 1492, 1459, 1374, 1222, 1111, 1075, 771 cm<sup>-1</sup>. ESI-MS:  $m/z = 359 [M + Na]^+$ . [(Z)-4-Hydroxybut-1-en-1-yl]tetrahydrospiro(cyclohexane-1,2'-furo[2,3-d][1,3]dioxol)-6'-ol(1a):  $[\alpha]_D^{25}$ -22.5

hexane-1,2'-furo[2,3-d][1,3]dioxol)-6'-ol (1a):  $[\alpha]_D^{25}-22.5$ (c 0.5, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 1.35-1.74$ (m, 10 H), 2.32–2.52 (m, 2 H), 3.66–3.80 (m, 2 H), 4.20 (d, J = 2.2 Hz, 1 H), 4.57 (d, J = 3.7 Hz, 1 H), 4.95 (dd, J = 2.2, 3.0 Hz, 1 H), 5.60–5.77 (m, 2 H), 5.97 (d, J = 3.7 Hz, 1 H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 23.5$ , 23.9, 24.8, 31.7, 35.8, 36.4, 61.3, 77.2, 78.0, 84.7, 103.9, 112.1, 126.5, 131.2. IR (neat): 3421, 2934, 2858, 1655, 1111, 1069, 1013, 953, 802 cm<sup>-1</sup>. ESI–MS: m/z = 293 [M + Na]<sup>+</sup>. HRMS: m/z [M + Na]<sup>+</sup> calcd for C<sub>14</sub>H<sub>22</sub>O<sub>5</sub>: 293.1359; found: 293.1353. {(*E*)-[5-(4-Hydroxy-but-1-enyl)-2,2-dimethyl]tetrahydrofuro[2,3-d][1,3]dioxol}-6-ol (1b):  $[\alpha]_D^{25}-42.2$  (*c* 0.61, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 1.20-1.33$  (m, 6 H), 2.42–2.51 (m, 1 H), 3.61–3.79 (m, 2 H), 4.12 (d, J = 2.6 Hz, 1 H), 4.51 (d, J = 3.7 Hz, 1 H), 4.84–4.91 (m, 1 H), 5.55–5.72 (m, 2 H), 5.89 (d, J = 3.5 Hz, 1 H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 26.1, 26.7, 31.6, 61.2, 76.3, 77.9, 85.2,

104.3, 111.4, 126.4, 131.2. IR (neat): 3363, 2978, 2927, 1376, 1248, 1217, 1163, 1071, 1008, 946 cm<sup>-1</sup>. ESI–MS: m/z = 230 [M + Na]<sup>+</sup>. HRMS: m/z calcd for C<sub>11</sub>H<sub>18</sub>O<sub>5</sub>: 253.1044 [M + Na]<sup>+</sup>; found: 253.1046.