

# Scope and Limitations of the Photooxidations of 2-( $\alpha$ -hydroxyalkyl) furans: Synthesis of 2-Hydroxy-*exo*-brevicomin

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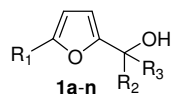
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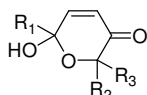
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## Part A: Experimental procedures



The photooxidation precursors, furanols **1a-n** shown in Scheme 3, were easily prepared using well-established known synthetic protocols. In particular, primary alcohols **1a**, **1e** and **1j** were prepared by NaBH<sub>4</sub> reduction of the corresponding commercially available furfurals. Secondary alcohols **1b**, **1f** and **1k** were easily synthesized by *n*-BuLi addition to the same furfurals, while PhMgBr addition to 5-methylfurfural was used in the preparation of **1i**. Furanols **1c** and **1d** were prepared by addition of furyllithium, prepared by deprotonation of furan with *n*-BuLi, to 3-methyl-2-butenal and acetone, respectively. Similarly, addition of methylfuryllithium to acetone and 3-methyl-2-butenal affords furanols **1g** and **1h**, respectively. Finally, substrates **1l**, **1m** and **1n** were prepared by aldol condensation of the enolate of acetophenone, or ethyl acetate (LDA was used as base), to 5-methylfurfural or furfural.



A solution of furanols **1a-n** (0.5 mmol) in MeOH (10 mL) containing rose bengal as photosensitizer (10<sup>-4</sup> M) was placed in a test tube and cooled with an ice bath (~ 5 °C). Oxygen was bubbled through the solution immediately before and during its irradiation with a xenon Variac Eimac Cermac 300 W visible light lamp. Complete consumption of the starting material was observed by TLC after 4 mins irradiation.

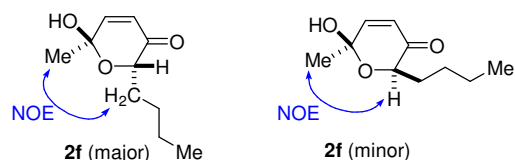
The reaction mixture was transferred to a round bottom flask and concentrated *in vacuo*. The residues was dissolved in CHCl<sub>3</sub>, concentrated once again *in vacuo* and left for 2 h under high vacuum to ensure complete removal of MeOH. The relative ratios of the MeOH trapping product, hydroperoxides **5** (Scheme 2), and fragmentation products **4** were measured at this stage by <sup>1</sup>H NMR. The crude mixture of hydroperoxides **5** and fragmentation product **4** was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (4 mL) and an excess of Me<sub>2</sub>S (100 μL) was then added. The solution was stirred for 15 h at room temperature, after which time the DMS/DMSO ratio as well as the amount of MeOH

produced remained unchanged (based on  $^1\text{H}$  NMR monitoring when  $\text{CDCl}_3$  instead of  $\text{CH}_2\text{Cl}_2$  was used as solvent). The relative ratios of the desired pyranones **2** and fragmentation products 4-hydroxybutenolides **4** were measured at this stage by  $^1\text{H}$  NMR, and, as expected, were very close to the **5:4** ratio measured above.

The reaction solution was concentrated in *vacuo* and purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 5:1  $\rightarrow$  1:1) to afford pure 6-hydroxy-3(2*H*)-pyranones **2** (45% for **2a**, 85% for **2e**, 71% for **2f**, 48% for **2g**, 63% for **2j**, 79% for **2l** and 77% for **2m**).

**2a**:  $^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 6.97 (dd,  $J_1$  = 10.4 Hz,  $J_2$  = 3.0 Hz, 1H), 6.17 (d,  $J$  = 10.4 Hz, 1H), 5.64 (d,  $J$  = 3.0 Hz, 1H), 4.58 (d,  $J$  = 16.9 Hz, 1H), 4.14 (d,  $J$  = 16.9 Hz, 1H) ppm;  $^{13}\text{C}$  (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 194.6, 145.8, 127.9, 88.2, 66.6 ppm.

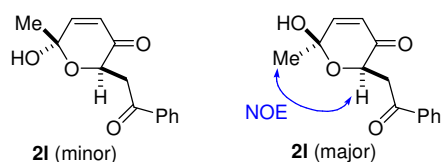
**2e**:  $^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 6.85 (d,  $J$  = 10.3 Hz, 1H), 6.02 (d,  $J$  = 10.3 Hz, 1H), 4.55 (d,  $J$  = 16.9 Hz, 1H), 4.08 (d,  $J$  = 16.9 Hz, 1H), 1.61 (s, 3H) ppm;  $^{13}\text{C}$ -NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 195.1, 149.3, 126.2, 92.6, 66.5, 27.7 ppm.



**2f**: Mixture of two diastereoisomers in 8:1 ratio. Based on the NOE studies shown above the *trans*-diastereoisomer is the major one.  $^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ ) for the major diastereoisomer:  $\delta$  = 6.80 (d,  $J$  = 10.2 Hz, 1H), 6.01 (d,  $J$  = 10.2 Hz, 1H), 4.50 (dd,  $J_1$  = 7.8 Hz,  $J_2$  = 3.9 Hz, 1H), 2.62 (s, -OH), 1.91 (m, 1H), 1.65 (m, 1H), 1.63 (s, 3H), 1.35 (m, 4H), 0.90 (t,  $J$  = 7.0 Hz, 3H) ppm;  $^{13}\text{C}$ -NMR (75 MHz,  $\text{CDCl}_3$ ) for the major diastereoisomer:  $\delta$  = 196.9, 147.7, 126.6, 92.7, 74.3, 29.3, 29.0, 27.1, 22.5, 14.0 ppm; HRMS (TOFMS EI<sup>+</sup>): calcd for  $\text{C}_{10}\text{H}_{16}\text{O}_3$ : 184.1099  $[\text{M}]^+$ ; found: 184.1097.

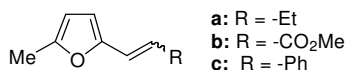
**2g**:  $^1\text{H}$ -NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 6.81 (d,  $J$  = 10.0 Hz, 1H), 6.00 (d,  $J$  = 10.0 Hz, 1H), 1.66 (s, -OH), 1.60 (s, 3H), 1.53 (s, 3), 1.36 (s, 3H) ppm;  $^{13}\text{C}$ -NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 199.3, 147.5, 124.3, 92.6, 78.8, 30.5, 28.0, 25.9 ppm; HRMS (TOFMS ES<sup>+</sup>): calcd for  $\text{C}_8\text{H}_{12}\text{O}_3\text{Na}$ : 179.0684  $[\text{M} + \text{Na}]^+$ ; found: 179.0670.

**2j:** This compound appears as a 1.1:1 mixture of the closed (hemiketal) and the open (1,4-enedione) form in  $\text{CDCl}_3$ .  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ , *open form*):  $\delta$  = 7.93 (d,  $J$  = 7.1 Hz, 2H), 7.64 (m, 3H), 7.03 (d,  $J$  = 12.1 Hz, 1H), 6.56 (d,  $J$  = 12.1 Hz, 1H), 4.39 (brs, 2H), ppm;  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ , *closed form*):  $\delta$  = 7.51 (d,  $J$  = 7.8 Hz, 2H), 7.43 (m, 3H), 6.94 (d,  $J$  = 10.2 Hz, 1H), 6.10 (d,  $J$  = 10.2 Hz, 1H), 4.74 (d,  $J$  = 16.7 Hz, 1H), 4.28 (d,  $J$  = 16.7 Hz, 1H) ppm;  $^{13}\text{C-NMR}$  (75 MHz,  $\text{CDCl}_3$ , *both open and closed forms*):  $\delta$  = 200.2, 194.2, 192.9, 148.7, 141.6, 138.4, 135.4, 134.1, 131.4, 129.3, 128.9 (2C), 128.7 (2C), 128.6 (2C), 126.0, 125.6 (2C), 94.0, 68.3, 66.8 ppm; HRMS (TOFMS EI<sup>+</sup>): calcd for  $\text{C}_{11}\text{H}_8\text{O}_2$ : 172.0524  $[\text{M} - \text{H}_2\text{O}]^+$ ; found: 172.0530.



**2l:** Mixture of two diastereoisomers in 8:1 ratio. Based on the NOE studies shown above the *cis*-diastereoisomer is the major one.  $^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ ) *for the major diastereoisomer*:  $\delta$  = 7.95 (d,  $J$  = 7.5 Hz, 2H), 7.57 (t,  $J$  = 7.5 Hz, 1H), 7.46 (t,  $J$  = 7.5 Hz, 2H), 6.85 (d,  $J$  = 10.0 Hz, 1H), 6.10 (d,  $J$  = 10.0 Hz, 1H), 5.25 (dd,  $J_1$  = 7.5 Hz,  $J_2$  = 3.0 Hz, 1H), 3.68 (dd,  $J_1$  = 17.5 Hz,  $J_2$  = 3.0 Hz, 1H), 3.37 (dd,  $J_1$  = 17.5 Hz,  $J_2$  = 7.5 Hz, 1H), 1.60 (s, 3H) ppm;  $^{13}\text{C-NMR}$  (75 MHz,  $\text{CDCl}_3$ ) *for the major diastereoisomer*:  $\delta$  = 196.8, 196.2, 148.2, 136.5, 133.4, 128.6 (2C), 128.2 (2C), 126.0, 93.1, 70.7, 39.1, 28.6; HRMS (TOFMS ES<sup>+</sup>): calcd for  $\text{C}_{14}\text{H}_{14}\text{O}_4\text{Na}$ : 269.0790  $[\text{M} + \text{Na}]^+$ ; found: 269.0783.

**2m:**  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 6.83 (d,  $J$  = 10.2 Hz, 1H), 6.06 (d,  $J$  = 10.2 Hz, 1H), 4.98 (dd,  $J_1$  = 7.6 Hz,  $J_2$  = 4.0 Hz, 1H), 4.16 (q,  $J$  = 7.1 Hz, 2H), 3.00 (dd,  $J_1$  = 16.8 Hz,  $J_2$  = 4.0 Hz, 1H), 2.69 (dd,  $J_1$  = 16.8 Hz,  $J_2$  = 7.6 Hz, 1H), 1.62 (s, 3H), 1.26 (t,  $J$  = 7.1 Hz, 3H) ppm;  $^{13}\text{C-NMR}$  (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 195.1, 170.9, 148.0, 126.0, 93.0, 71.2, 60.9, 35.2, 28.7, 14.1 ppm; HRMS (TOFMS ES<sup>+</sup>): calcd for  $\text{C}_{10}\text{H}_{14}\text{O}_5\text{Na}$ : 237.0739  $[\text{M} + \text{Na}]^+$ ; found: 237.0742.



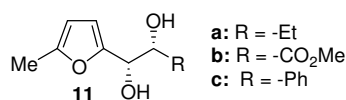
To a mixture of the phosphonium salt (the precursors of ylides **10a** or **10c**, 5.0 mmol) in anhydrous THF (20 mL) at 0 °C, was added a solution of *n*-BuLi (3.12 mL, 1.6 M in hexane, 5 mmol). The reaction mixture was warmed to room temperature and stirred for 1 h after which time all the phosphonium salt had been consumed. The red colored solution was re-cooled to 0 °C and a solution of 5-methylfurfural (**9**, 0.55 g, 5 mmol) in anhydrous THF (5 mL) was added. The reaction was warmed to room temperature, stirred for 3 h, concentrated to half its previous volume and then diluted with petroleum ether (50 mL). The Ph<sub>3</sub>P=O that was precipitated was removed by filtration and the remaining solution was concentrated in *vacuo* and purified by column chromatography (silica gel, petroleum ether:EtOAc = 1:0 → 50:1) to afford a mixture of olefins (*cis:trans* = 1.3:1, 0.51 g, 75 % for R = -Et, while *cis:trans* = 1.5:1, 0.75 g, 81 % for R = -Ph).

**For R = -Et:** <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ = 6.25 - 5.97 (m, 4H for trans plus 3H for cis), 5.53 (td, *J*<sub>1</sub> = 11.8, *J*<sub>2</sub> = 7.3, 1H for cis), 2.53 (df, *J*<sub>1</sub> = 7.3, *J*<sub>2</sub> = 1.7, 2H for cis), 2.37 (s, 3H for cis), 2.35 (s, 3H for trans), 2.27 (m, 2H for trans), 1.17 (t, *J* = 7.5, 3H for cis), 1.15 (t, *J* = 7.5, 3H for trans); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) *for cis isomer*: δ = 151.7, 150.9, 131.4, 116.9, 109.7, 107.1, 22.6, 14.0, 13.6 ppm; <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) *for trans isomer*: δ = 151.8, 151.0, 129.9, 117.7, 107.0, 106.9, 25.7, 13.5, 13.5 ppm.

**For R = -Ph:** <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ = 7.44 (m, 2H for cis plus 2H for trans), 7.33 (m, 2H for cis plus 2H for trans), 7.25 (tt, *J*<sub>1</sub> = 7.1 Hz, *J*<sub>2</sub> = 1.3 Hz, 1H for cis plus 1H for trans), 6.97 (d, *J* = 16.2 Hz, 1H for trans), 6.84 (d, *J* = 16.2 Hz, 1H for trans), 6.39 (d, *J* = 12.7 Hz, 1H for cis), 6.30 (d, *J* = 12.7 Hz, 1H for cis), 6.24 (d, *J* = 3.1 Hz, 1H for trans), 6.16 (d, *J* = 3.2 Hz, 1H for cis), 6.02 (dd, *J*<sub>1</sub> = 3.1 Hz, *J*<sub>2</sub> = 0.9 Hz, 1H for trans), 5.91 (brd, *J* = 3.2 Hz, 1H for cis), 2.36 (s, 3H for trans), 2.26 (s, 3H for cis); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) *for cis isomer*: δ = 151.6, 150.5, 137.3, 128.7 (2C), 128.0 (2C), 127.1, 126.1, 118.2, 111.0, 107.4, 13.6 ppm; <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) *for trans isomer*: δ = 152.3, 151.7, 137.6, 128.6 (2C), 127.2, 126.4 (2C), 125.4, 116.7, 109.9, 107.8, 13.8 ppm.

To a solution of 5-methylfurfural (**9**, 0.55 g, 5.0 mmol) at room temperature in anhydrous  $\text{CH}_2\text{Cl}_2$  (15 mL) was added the stabilized ylide **10b** (1.84 g, 5.5 mmol). The reaction mixture was stirred, at the same temperature, for 14 hours, concentrated to half its previous volume and then diluted with petroleum ether (30 mL). The  $\text{Ph}_3\text{P}=\text{O}$  that was precipitated was removed by filtration and the remaining solution was concentrated *in vacuo* and purified by column chromatography (silica gel, petroleum ether:EtOAc = 40:1  $\rightarrow$  30:1) to afford the desired *trans* ester (0.74 g, 89 %).

**For R = -CO<sub>2</sub>Me:** <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.35 (d,  $J$  = 15.7 Hz, 1H), 6.49 (d,  $J$  = 3.2 Hz, 1H), 6.22 (d,  $J$  = 15.7 Hz, 1H), 6.06 (dd,  $J_1$  = 3.2 Hz,  $J_2$  = 0.9 Hz, 1H), 3.76 (s, 3H), 2.33 (s, 3H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 167.8, 155.5, 149.5, 131.3, 116.5, 113.5, 108.8, 51.5, 13.9 ppm

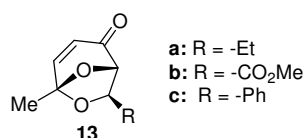


To a solution of each one of the three previously prepared olefins (2.0 mmol) in *t*-BuOH:H<sub>2</sub>O (12 mL:12 mL), at 0 °C, were added 190 mg (2.0 mmol) of methanesulfonyl amide and 2.0 g AD-mix- $\beta$  (in three portions, one every 6 h). The reaction mixture was stirred for 24 h at the same temperature until complete consumption of the starting material was observed by TLC. EtOAc (15 mL) was then added followed by Na<sub>2</sub>SO<sub>3</sub> (4.0 g) and the stirring was continued for 1 h until complete separation of the two phases was seen. The phases were separated and the aqueous phase was re-extracted with EtOAc (15 mL). The combined organic phases were dried with Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. Flash column chromatography (silica gel, petroleum ether:EtOAc = 10:1  $\rightarrow$  2:1) afforded pure 1,2-diols **11a** (exclusively *threo*, 231 mg, 68 %), **11b** (exclusively *threo*, 312 mg, 78 %) and **11c** (*threo*:*erythro* = 4:1, 283 mg, 65 %).

**11a:** <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 6.14 (d,  $J$  = 3 Hz, 1H), 5.88 (m, 1H), 4.35 (d,  $J$  = 6.8 Hz, 1H), 3.75 (m, 1H), 3.49 (brs, -OH), 3.19 (brs, -OH), 2.24 (s, 3H), 1.38 (m, 2H), 0.91 (t,  $J$  = 7.4 Hz, 3H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 152.2, 151.7, 108.3, 106.0, 74.7, 70.8, 25.7, 13.4, 9.8 ppm; HRMS (TOFMS ES<sup>+</sup>): calcd for C<sub>9</sub>H<sub>14</sub>O<sub>3</sub>Na: 193.0841 [M + Na]<sup>+</sup>; found: 193.0838.

**11b:**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 6.24 (d,  $J$  = 3.1 Hz, 1H), 5.90 (dd,  $J_1$  = 3.1 Hz,  $J_2$  = 0.8 Hz, 1H), 4.94 (brs, 1H), 4.48 (d,  $J$  = 2.5 Hz, 1H), 3.80 (s, 3H), 3.55 (brs, -OH), 3.23 (brs, -OH), 2.25 (s, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 172.8, 152.0, 150.9, 108.3, 106.2, 72.7, 68.9, 52.8, 13.4 ppm; HRMS (TOFMS ES+): calcd for  $\text{C}_9\text{H}_{12}\text{O}_5\text{Na}$ : 223.0582  $[\text{M} + \text{Na}]^+$ ; found: 223.0580.

**11c:**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ) for *threo* diastereoisomer:  $\delta$  = 7.23 (m, 5H), 5.93 (d,  $J$  = 3.1 Hz, 1H), 5.79 (dd,  $J_1$  = 3.1,  $J_2$  = 0.8, 1H), 4.90 (d,  $J$  = 7.4, 1H), 4.55 (d,  $J$  = 7.4, 1H), 3.58 (brs, 2 -OH), 2.23 (d,  $J$  = 0.8, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ) for *threo* diastereoisomer:  $\delta$  = 151.7, 150.7, 140.0, 128.0 (2C), 127.7, 126.5 (2C), 109.1, 106.0, 75.8, 72.4, 13.4 ppm; HRMS (TOFMS ES+): calcd for  $\text{C}_{13}\text{H}_{14}\text{O}_3\text{Na}$ : 241.0841  $[\text{M} + \text{Na}]^+$ ; found: 241.0836.



A solution of furan-diols **11a-c** (0.5 mmol) in MeOH (10 mL) containing rose bengal as photosensitizer ( $10^{-4}$  M) was placed in a test tube and cooled with an ice bath ( $\sim 5^\circ\text{C}$ ). Oxygen was bubbled through the solution immediately before and during its irradiation with a xenon Variac Eimac Cermox 300 W visible light lamp. Complete consumption of the starting material was observed by TLC after 4 mins irradiation.

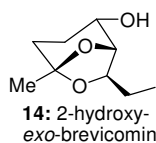
The reaction mixture was transferred to a round bottom flask and concentrated *in vacuo*. The residue was dissolved in  $\text{CHCl}_3$ , concentrated once again *in vacuo* and was left for 2 h under high vacuum to ensure complete removal of MeOH. The relative ratios of the MeOH trapping product hydroperoxides **5** (Scheme 2) and fragmentation products **4e** were measured at this stage by  $^1\text{H}$  NMR. The crude mixture of hydroperoxides **5** and fragmentation product **4e** was dissolved in  $\text{CH}_2\text{Cl}_2$  (4 mL), an excess of  $\text{Me}_2\text{S}$  (100  $\mu\text{L}$ ) was then added and the solution was stirred for 15 h at room temperature. Catalytic amount (5 mg) of *p*-TsOH was then added and the solution was stirred for 3 more hours at room temperature and concentrated *in vacuo*. The relative ratios of the desired 6,8-dioxabicyclo[3.2.1]oct-3-en-2-ones **13a-c** and fragmentation products 4-hydroxybutenolides **4e** were also measured at this stage by  $^1\text{H}$  NMR, and, as expected, were very close to the **5:4e** ratio measured above. The

reaction was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 15:1  $\rightarrow$  5:1) to afford pure 6,8-dioxabicyclo[3.2.1]oct-3-en-2-ones **13a** (44 mg, 53 %), **13b** (74 mg, 75 %) and **13c** (10:1 mixture of two diastereoisomers, 65 mg, 60 %).

**13a:**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 6.95 (d,  $J$  = 9.7 Hz, 1H), 6.00 (dd,  $J_1$  = 9.7 Hz,  $J_2$  = 1.5 Hz, 1H), 4.33 (t,  $J$  = 1.5 Hz, 1H), 3.75 (dt,  $J_1$  = 6.3 Hz,  $J_2$  = 1.5 Hz, 1H), 1.70 (m, 2H), 1.69 (s, 3H), 0.98 (t,  $J$  = 7.4 Hz, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 195.1, 150.8, 125.7, 103.6, 84.1, 77.1, 27.2, 21.9, 9.6 ppm.

**13b:**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.07 (d,  $J$  = 9.7 Hz, 1H), 6.06 (dd,  $J_1$  = 9.7 Hz,  $J_2$  = 1.3 Hz, 1H), 4.89 (t,  $J$  = 1.3 Hz, 1H), 4.30 (d,  $J$  = 1.3 Hz, 1H), 3.82 (s, 3H), 1.81 (s, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 192.5, 169.3, 151.3, 126.1, 105.5, 84.0, 73.5, 53.0, 21.6 ppm; HRMS (TOFMS EI $^+$ ): calcd for  $\text{C}_9\text{H}_{10}\text{O}_5$ : 198.0528  $[\text{M}]^+$ ; found: 198.0535.

**13c:**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ) for major diastereoisomer:  $\delta$  = 7.36 (m, 5H), 7.08 (d,  $J$  = 9.8 Hz, 1H), 6.10 (dd,  $J_1$  = 9.8 Hz,  $J_2$  = 1.6 Hz, 1H), 4.82 (d,  $J$  = 1.4 Hz, 1H), 4.52 (t,  $J$  = 1.4 Hz, 1H), 1.87 (s, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ) for major diastereoisomer:  $\delta$  = 194.3, 151.0, 138.8, 128.7 (2C), 128.5, 126.2 (2C), 125.7, 104.6, 87.4, 77.5, 21.7 ppm; HRMS (TOFMS ES $^+$ ): calcd for  $\text{C}_{13}\text{H}_{12}\text{O}_3\text{Na}$ : 239.0684  $[\text{M} + \text{Na}]^+$ ; found: 239.0679.



To a solution of 6,8-dioxabicyclo[3.2.1]oct-3-en-2-one **13a** (30 mg, 0.18 mmol) in MeOH (3 mL), at 0 °C, was added  $\text{NaBH}_4$  (20 mg, 0.53 mmol) and the reaction was stirred at the same temperature for 20 min. Water (3 mL) was added and the aqueous phase was extracted with  $\text{Et}_2\text{O}$  (2 x 5 mL). The combined organic phases were dried with  $\text{MgSO}_4$  and concentrated *in vacuo* to afford the corresponding pure allylic alcohol (29 mg, 95 %).

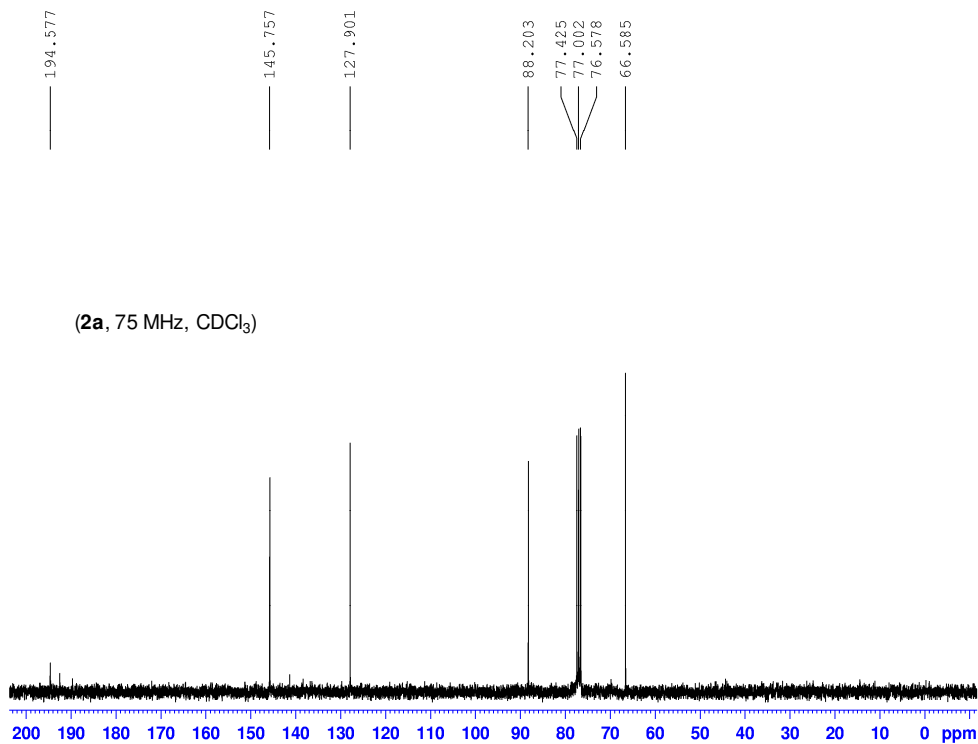
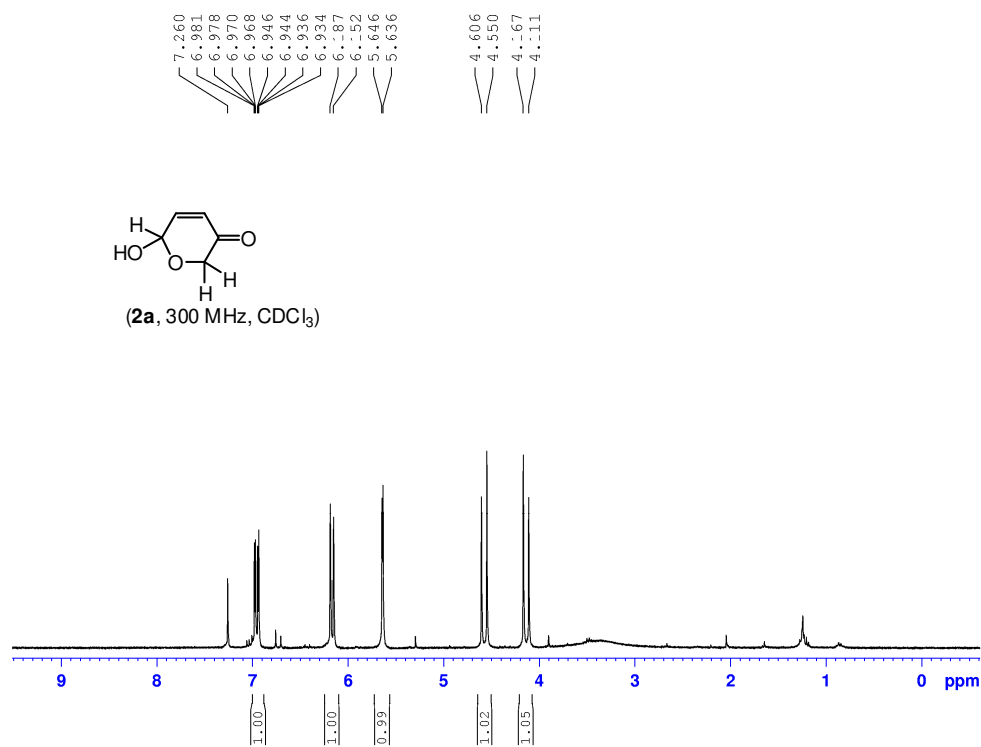
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 5.78 (dd,  $J_1$  = 9.6 Hz,  $J_2$  = 1.6 Hz, 1H), 5.65 (td,  $J_1$  = 9.6 Hz,  $J_2$  = 1.9 Hz, 1H), 4.71 (m, 1H), 4.17 (dt,  $J_1$  = 6.3 Hz,  $J_2$  = 1.7 Hz, 1H), 4.08

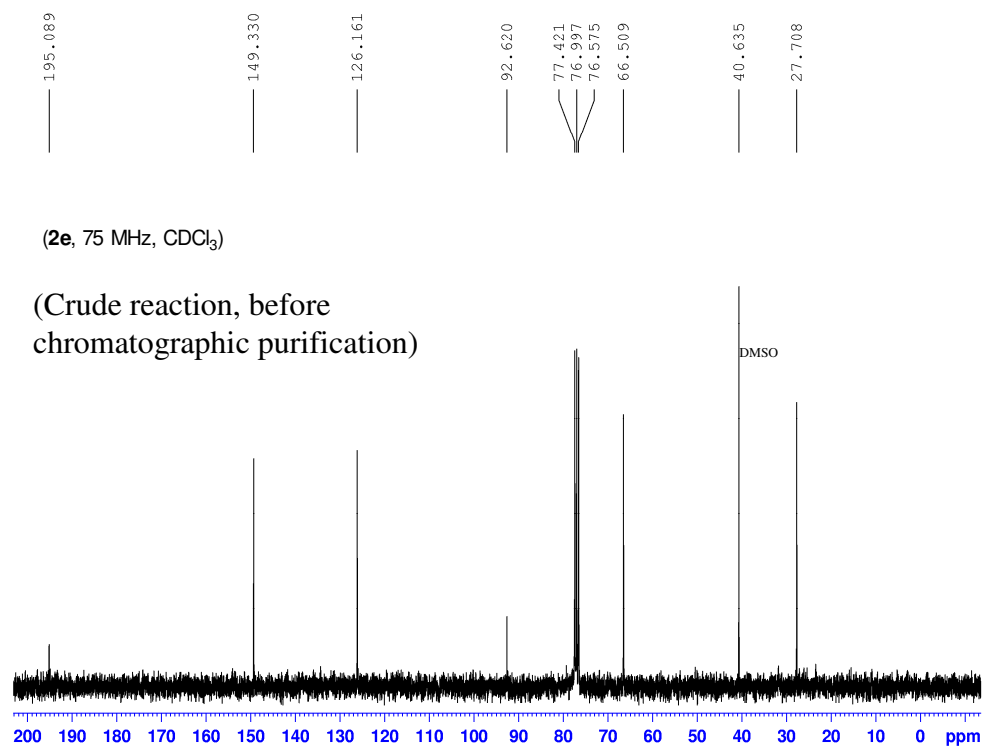
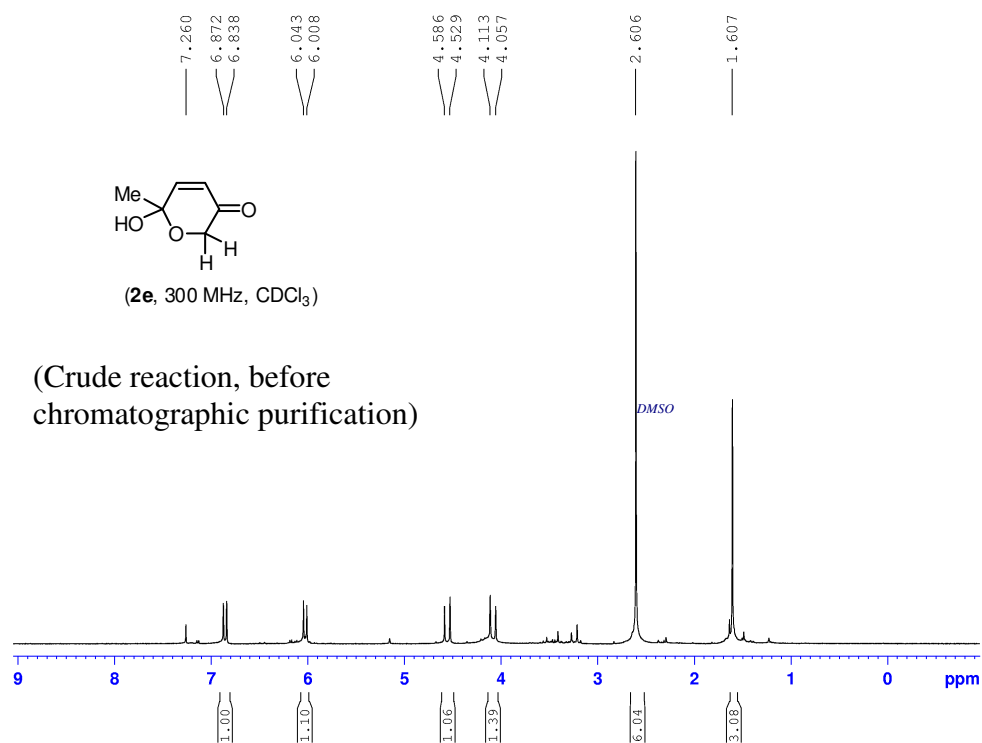


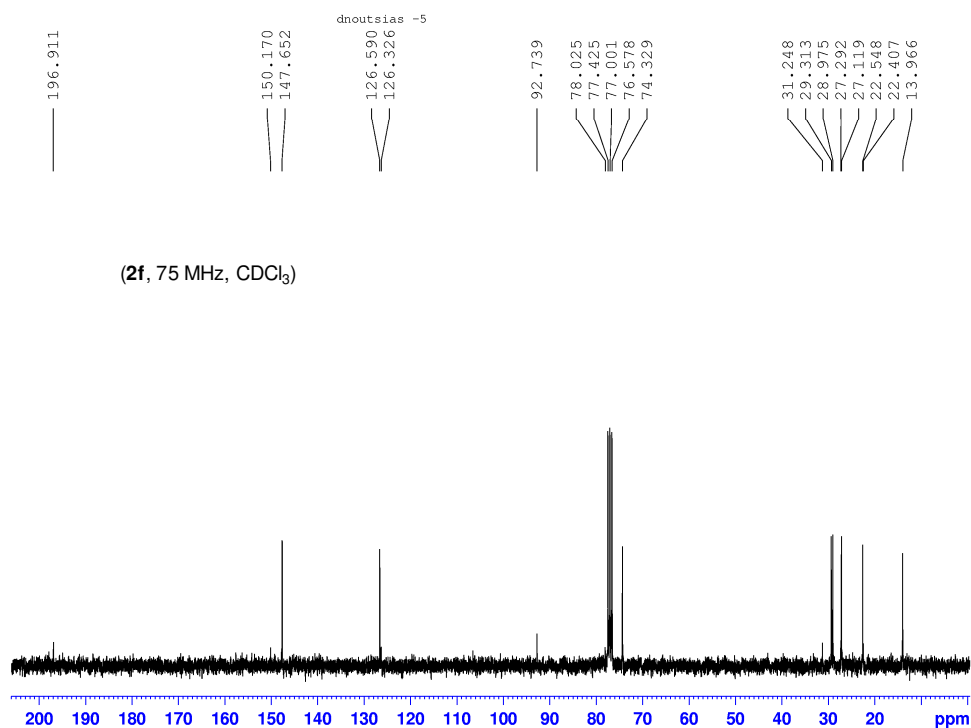
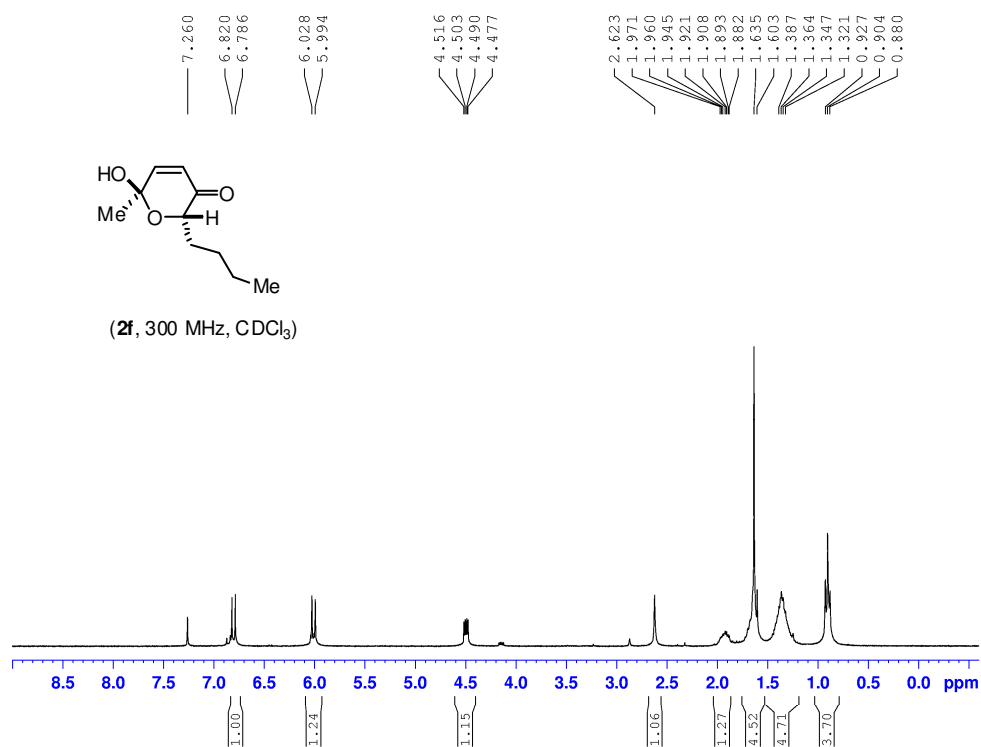
(m, 1H), 1.70 – 1.55 (m, 2H), 1.53 (s, 3H), 1.25 (s, -OH), 0.96 (t,  $J = 7.4$  Hz, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta = 131.9, 128.0, 102.6, 80.2, 75.7, 67.1, 27.4, 23.3, 9.4$  ppm.

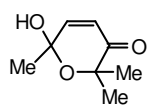
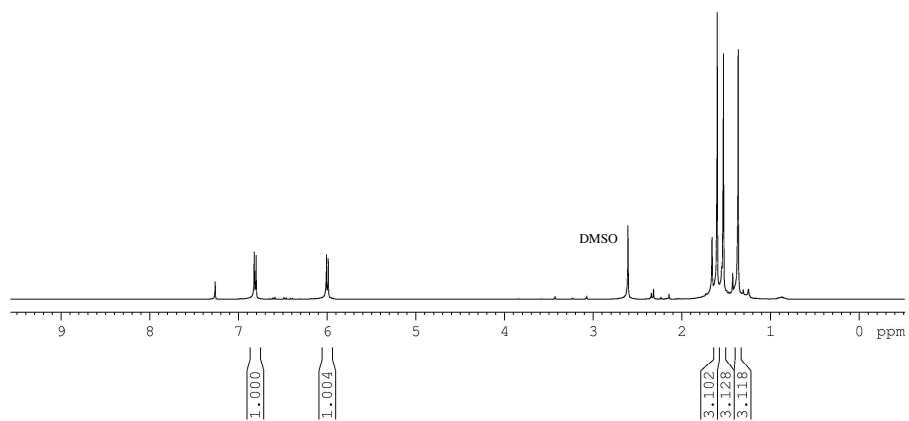
A solution of the above prepared allylic alcohol (29 mg, 0.17 mmol) in dry EtOAc (3 mL) had  $\text{H}_2$  bubbled through it for 20 min. Pd/C (30 mg, 10 wt%) was then added and two balloons of  $\text{H}_2$  were attached. The reaction mixture was stirred for 30 min at room temperature and then passed through a pad of *celite*. The *celite* was carefully washed with EtOAc (5 mL) and the combined filtrates were concentrated *in vacuo*. The reaction was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 10:1  $\rightarrow$  4:1) to afford 2-hydroxy-*exo*-brevicommin (**14**, 25 mg, 85 %).

$[\alpha]_{\text{D}}^{20} = +38.6$  ( $c = 2.5$ ,  $\text{CHCl}_3$ ), lit.<sup>20d</sup>  $[\alpha]_{\text{D}}^{20} = +33.3$  ( $c = 1.94$ ,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (300 MHz,  $\text{C}_6\text{D}_6$ ):  $\delta = 4.15$  (t,  $J = 6.5$  Hz, 1H), 3.75 (d,  $J = 3.6$  Hz, 1H), 3.56 (m, 1H), 1.65 – 1.43 (m, 6H), 1.45 (s, 3H), 0.90 (t,  $J = 7.5$  Hz, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta = 106.9, 80.5, 77.3, 66.3, 35.0, 28.3, 26.7, 23.9, 9.7$  ppm.

**Part B: Copies of  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR spectra**





(2g, 500 MHz, CDCl<sub>3</sub>)

199.341

147.530

124.341

92.567

78.766

77.425

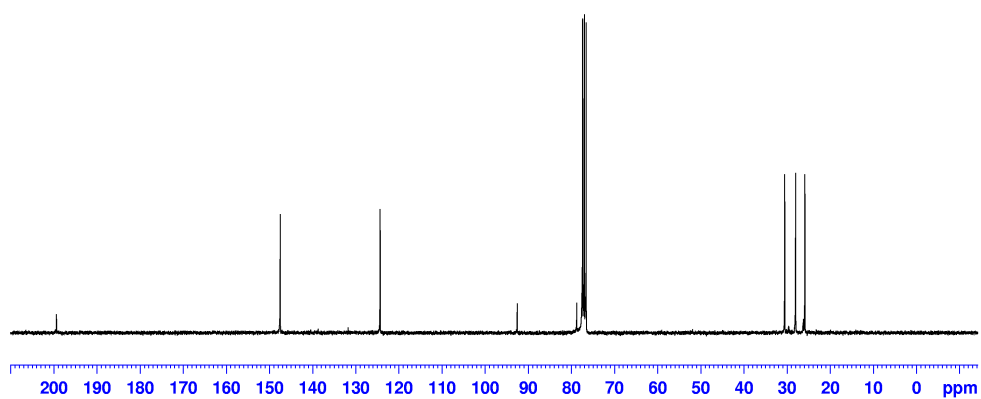
77.001

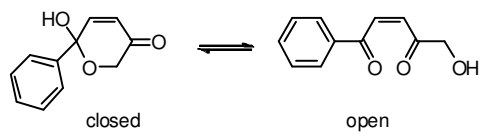
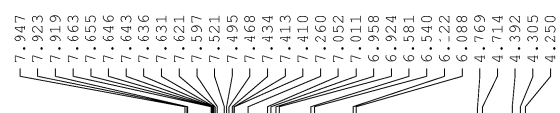
76.578

30.529

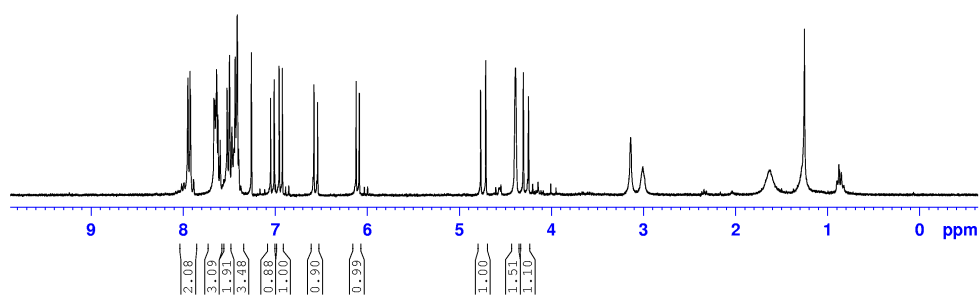
28.023

25.854

(2g, 75 MHz, CDCl<sub>3</sub>)



(**2j**, 300 MHz, CDCl<sub>3</sub>)



(**2j**, 300 MHz, CDCl<sub>3</sub>, both open and closed forms)

