Synthesis of Natural Fimbrolides

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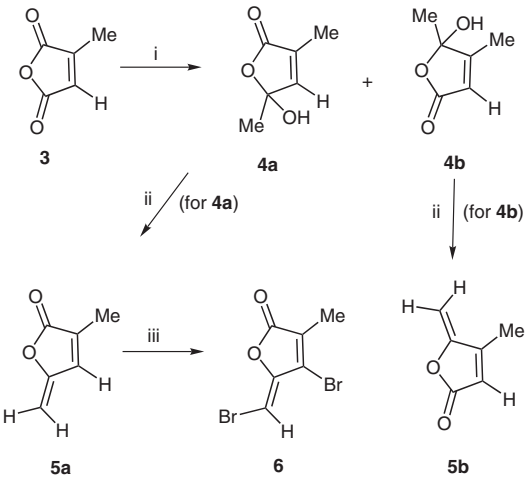
Abstract: Starting from citraconic anhydride, a three-step approach to fimbrolide congener is reported by taking the advantage of a regioselective Grignard reaction with an anhydride, followed by a dehydrative cyclization and double bromination–dehydrobromination sequence. Starting from *N*-(4-tolyl)maleimide, an eight-step synthesis of two natural fimbrolides is reported with good yields via the synthesis of requisite butylmaleic anhydride, its regioselective Grignard coupling reaction, and a bromination–dehydrobromination pathway.

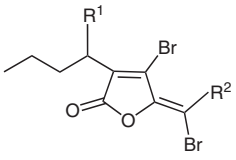
Key words: butylmaleic anhydride, regioselective Grignard coupling, butenolides, bromination, fimbrolides

Fimbrolides (**1**) have been isolated from the red marine algae *Delisea fimbriata*; they are bromobutenolides with interesting antifungal and antimicrobial properties.[1] Pulchralides (**2**) appear to be the [2+2] cycloadducts of the fimbrolides **1** and they have been isolated from antarctic macroalgae[2] (Figure 1). The natural fimbrolides **1** are limited in availability and to date four syntheses of **1** have been described in the literature by oxidative cyclodehydration of dibromo-2-butyllevulinic acid,[3,4] treatment of a suitable β-lithiocarboxylate with acetic anhydride as the key step,[5] and treatment of a γ-monosubstituted allenic ester with *N*-bromosuccinimide in water.[6] In continuation of our studies on the synthesis of structurally interesting and biologically important natural and unnatural products using cyclic anhydrides as potential precursors,[7] we herein report the synthesis of fimbrolides starting from *N*-arylmaleimide **7** via butylmaleic anhydride (**12**) (Schemes 1 and 2).

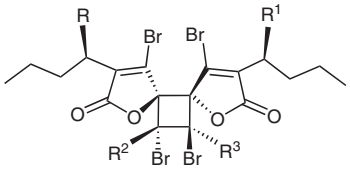


Scheme 1 Reagents and conditions: (i) MeMgI (1.10 equiv), Et_2O, –20 °C, 2 h (**4a**: 68%, **4b**: 8%); (ii) P_2O_5, benzene, reflux, 5 h (**5a**: 88%, **5b**: 85%); (iii) (a) Br_2 (2.20 equiv), CCl_4, 0 °C to r.t., 10 h, (b) Et_3N (2.20 equiv), $CHCl_3$, 0 °C to r.t., 5 h (68%).

We decided to use butylmaleic anhydride (**12**) as precursor for the synthesis of fimbrolides. To confirm the feasibility of our proposal, we initially used the readily available citraconic anhydride (**3**) for model studies (Scheme 1). The regioselective nucleophilic addition of methylmagnesium iodide to citraconic anhydride (**3**) at –20 °C furnished a mixture of lactols **4a** and **4b** in ~88:12 ratio with 76% yield. Separation of **4a** and **4b** by column chromatography (silica gel) followed by the phosphorus pentoxide induced dehydration gave the butenolides **5a** and **5b** in 88% and 85% yields, respectively. Reaction of compound **5a** with 2.20 equivalents of bro-



fimbrolide (**1a**): $R^1 = R^2 = H$
fimbrolide (**1b**): $R^1 = H$, $R^2 = Br$
acetoxyfimbrolide (**1c**): $R^1 = OAc$, $R^2 = H$
hydroxyfimbrolide (**1d**): $R^1 = OH$, $R^2 = H$



pulchralide A (**2a**): $R = R^1 = OAc$, $R^2 = R^3 = H$
pulchralide B (**2b**): $R = R^1 = R^2 = R^3 = H$
pulchralide C (**2c**): $R = OAc$, $R^1 = R^2 = R^3 = H$

Figure 1 Fimbrolides and pulchralides

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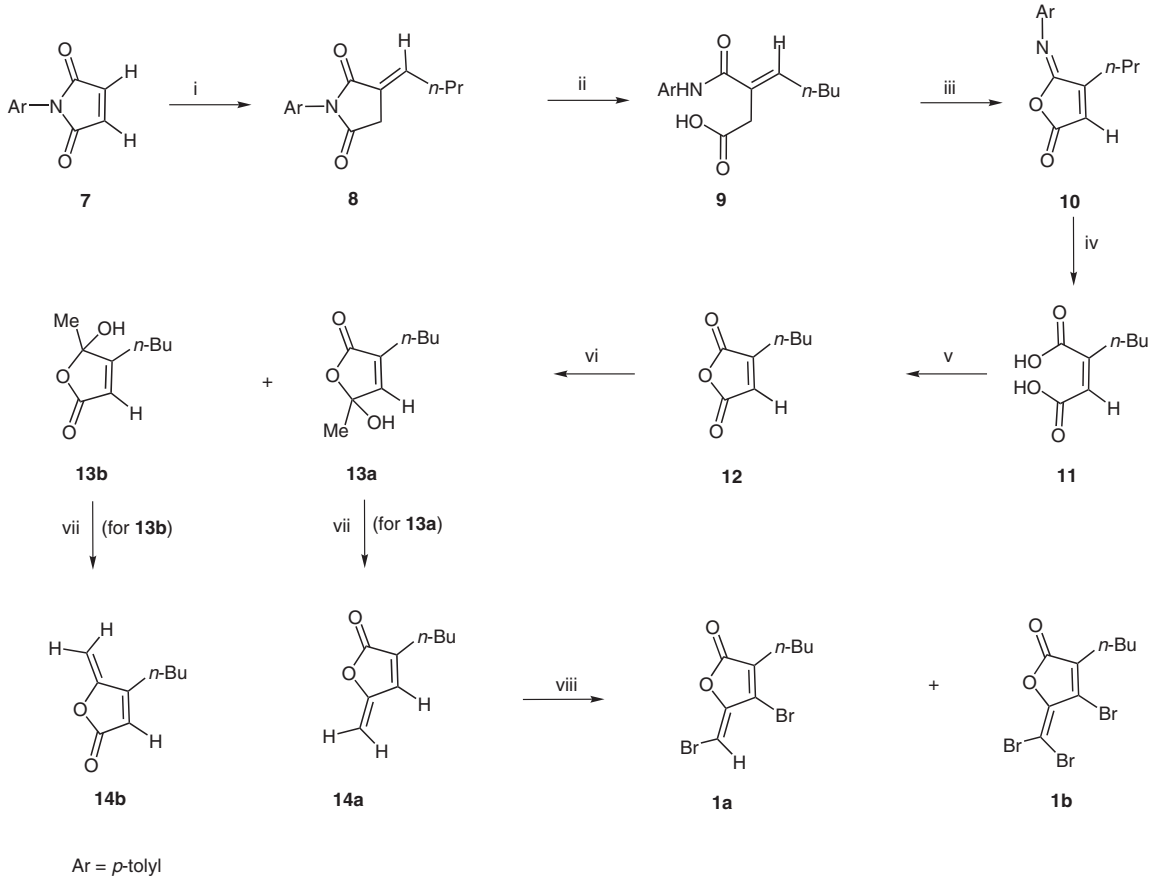

Scheme 2 Reagents and conditions: (i) Ph_3P (1.00 equiv), PrCHO (1.50 equiv), THF, reflux, 10 h (90%); (ii) aq 2 M LiOH, THF, 0 °C to r.t., 5 h (93%); (iii) cyanuric chloride (1.10 equiv), Et_3N (3.00 equiv), CH_2Cl_2, 0 °C to r.t., 8 h (85%); (iv) HCl–AcOH (1:1), reflux, 66 h (96%); (v) Ac_2O, 60 °C, 3 h (90%); (vi) MeMgI (1.10 equiv), Et_2O, –20 °C, 2 h (**13a**: 62%, **13b**: 9%); (vii) P_2O_5, benzene, reflux, 5 h (**14a**: 90%, **14b**: 87%); (viii) (a) Br_2 (2.20/3.30 equiv), CCl_4, 0 °C to r.t., 10 h, (b) Et_3N (2.20/3.30 equiv), $CHCl_3$, 0 °C to r.t., 5 h (**1a**: 37/15%, **1b**: 18/41%).

mine at 0 °C followed by the treatment with triethylamine, yielded exclusively the dibromobutenolide **6** in 68% yield, by the addition of two molecules of bromine to two different C=C bonds followed by a double dehydrobromination pathway.

We decided to prepare butylmaleic anhydride (**12**) using our own method[8] and obtained butylisomaleimide **10** from the maleimide **7** in three steps (Scheme 2). The acid-catalyzed hydrolysis of the isomaleimide **10** followed by acetic anhydride induced dehydrative cyclization of the thus-formed butylmaleic acid **11** gave the anhydride **12** in 90% yield. The regioselective reaction of methylmagnesium iodide with anhydride **12** at –20 °C again produced a mixture of lactols **13a** and **13b** in ~85:15 ratio with 71% yield. Herein, as expected, the nucleophilic addition of the Grignard reagent took place predominantly at the unhindered carbonyl carbon, thus providing **13a** as the major product. It was difficult for us to lower the temperature in order to achieve higher regioselectivity as below –20 °C the anhydride **12** started separating out as a sticky solid. Separation of **13a** and **13b** by column chromatography (silica gel) followed by phosphorus pentoxide induced dehydration gave the expected butenolides **14a** and **14b** in 90% and 87% yield, respectively. During the isolation of **14a** and **14b**, we noticed that the butenolides **14a** and **14b** are quite stable in organic solvents, but they have a propensity to undergo polymerization during the course of isolation and also in the neat form. The structural assignment of **14a** and **14b** was done on the basis of NMR spectral data and as expected the β-hydrogen in **14a** was more deshielded ($\delta = 7.03$) than the α-hydrogen in **14b** ($\delta = 5.99$). At this stage, to obtain the fimbrolides, we systematically studied the bromination reactions of **14a** at 0 °C with 2.20 and 3.30 equivalents of bromine in carbon tetrachloride. In these reactions, we always ended up with the formation of a mixture of the fimbrolides **1a** and **1b** via the addition–elimination pathway together with a quantity of gummy material. Using 2.20 equivalents of bromine, **1a** was formed as the major product, while **1b** was formed as the major product with the use of 3.30 equivalents of bromine. In these reactions, both the addition of bromine to the C=C bonds and the elimination of hydrogen bromide were instantaneous, but to ensure complete dehydrobromination, the use of triethylamine was necessary. Herein, all our attempts to obtain exclusively **1a** or **1b** met with failure and forced conditions resulted in the formation of a polymeric gum. Thus, the obtained mixture of **1a**, **1b**, and polymeric gum was initially filtered through a silica gel column to remove the impurities and then the remaining mixture of **1a** and **1b** was separat-

ed by HPLC using the known procedure.[1c] The analytical and spectral data obtained for **1a** and **1b** were in complete agreement with the reported data.[3–6] Starting from maleimide **7**, the fimbrolides **1a** and **1b** were obtained in eight steps with 13% and 14% overall yield, respectively. A reported attempt to convert fimbrolide into pulchralide photochemically was unsuccessful, thus supporting their biotic genesis.[2]

In summary, we have demonstrated a facile synthesis of two natural fimbrolides, starting from butylmaleic anhydride, taking the advantage of a regioselective Grignard coupling reaction and an instantaneous bromination–dehydrobromination process. We feel that our present approach is general in nature and will be useful for the synthesis of several other suitably substituted butyrolactone congeners for structure–activity relationship studies.

Commercially available citraconic anhydride, *p*-toluidine, P_2O_5, butyraldehyde, Ac_2O, MeI, Br_2, and Ph_3P were used. Freshly recrystallized cyanuric chloride (from CCl_4) was used. The petroleum ether (PE) used had boiling range 60–80 °C. Melting points are uncorrected. Column chromatographic separations were carried out on silica gel (60–120 mesh). FT-IR spectra were recorded on a FT-IR-8300 Shimadzu spectrometer. ^{1}H NMR spectra were recorded in $CDCl_3$ using TMS as internal standard and in DMSO-d_6 on a Bruker AC 200 NMR spectrometer (200 MHz). ^{13}C NMR spectra were recorded on Bruker AC 200, Bruker AC 400, and Bruker DRX 500 NMR spectrometers (50 MHz, 100 MHz, and 125 MHZ respectively).

5-Hydroxy-3,5-dimethylfuran-2(5*H*)-one (4a) and 5-Hydroxy-4,5-dimethylfuran-2(5*H*)-one (4b); Typical Procedure

A fresh soln of MeMgI in Et_2O was prepared as follows: A soln of MeI (1.40 g, 9.82 mmol) in anhyd Et_2O (30 mL) was added at 0 °C to Mg turnings (1.18 g, 49.10 mmol) in anhyd Et_2O (10 mL) under argon with constant stirring in 3 equal portions with 10-min intervals. The mixture was further stirred at 0 °C for 30 min. This freshly generated Grignard reagent was added in a dropwise fashion to a soln of citraconic anhydride (**3**, 1.00 g, 8.92 mmol) in anhyd Et_2O (15 mL) under argon atmosphere at –20 °C, and the mixture was further stirred at the same temperature for 2 h. The reaction was quenched by the addition of sat. aq NH_4Cl (20 mL) and EtOAc (50 mL) was added to the mixture. The separated organic layer was washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The obtained residue was purified by column chromatography (silica gel, PE–EtOAc, 9:1) to give **4a** (780 mg, 68%) and **4b** (90 mg, 8%).

4a

Colorless solid; mp 98–99 °C (PE–EtOAc).

IR ($CHCl_3$): 3385, 1767, 1751, 1709 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.63 (s, 3 H), 1.85 (d, *J* = 2 Hz, 3 H), 5.01 (br s, 1 H), 6.84 (q, *J* = 2 Hz, 1 H).

Anal. Calcd for $C_6H_8O_3$: C, 56.25; H, 6.29. Found: C, 56.31; H, 6.13.

4b

Yellowish thick oil.

IR (neat): 3354, 1744, 1670, 1647 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.64 (s, 3 H), 2.09 (d, *J* = 2 Hz, 3 H), 4.96 (br s, 1 H), 5.74 (q, *J* = 2 Hz, 1 H).

Anal. Calcd for $C_6H_8O_3$: C, 56.25; H, 6.29. Found: C, 56.09; H, 6.22.

3-Methyl-5-methylenefuran-2(5*H*)-one (5a); Typical Procedure

A suspension of **4a** (700 mg, 5.47 mmol) and P_2O_5 (2.33 g, 16.41 mmol) in benzene (20 mL) was refluxed for 5 h. The mixture was filtered through Celite and the residue was washed with benzene (2 × 20 mL). The organic layer was concentrated in vacuo and the obtained crude product was purified by column chromatography (silica gel, PE–EtOAc, 9:1) to give **5a** (530 mg, 88%) as a yellowish thick oil.

IR ($CHCl_3$): 1771, 1653 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.03 (d, *J* = 2 Hz, 3 H), 4.77 (d, *J* = 4 Hz, 1 H), 5.11 (t, *J* = 2 Hz, 1 H), 7.06 (d, *J* = 2 Hz, 1 H).

Anal. Calcd for $C_6H_6O_2$: C, 65.45; H, 5.49. Found: C, 65.32; H, 5.55.

4-Methyl-5-methylenefuran-2(5*H*)-one (5b)

Obtained using the typical procedure for **5a** as a yellowish thick oil; yield: 85%.

IR ($CHCl_3$): 1767, 1655 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.18 (d, *J* = 2 Hz, 3 H), 4.91 (dd, *J* = 4, 1 Hz, 1 H), 5.15 (dd, *J* = 4, 2 Hz, 1 H), 6.00 (sextet, *J* = 2 Hz, 1 H).

Anal. Calcd for $C_6H_6O_2$: C, 65.45; H, 5.49. Found: C, 65.51; H, 5.53.

(*Z*)-4-Bromo-5-(bromomethylene)-3-methylfuran-2(5*H*)-one (6); Typical Procedure

A soln of Br_2 (0.21 mL, 3.99 mmol) in CCl_4 (5 mL) was added to the soln of **5a** (200 mg, 1.82 mmol) in CCl_4 (10 mL) at 0 °C. The mixture was stirred at r.t. for 10 h and then the solvent was removed in vacuo. The obtained residue was dissolved in $CHCl_3$ and Et_3N (0.56 mL, 3.99 mmol) was added at 0 °C. The mixture was further stirred at r.t. for 5 h. The solvent was removed in vacuo and the obtained crude product was purified by column chromatography (silica gel, PE–EtOAc) to give pure **6** (330 mg, 68%) as a colorless solid; mp 69–70 °C (PE–EtOAc).

IR ($CHCl_3$): 1786, 1638, 1609 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.16 (s, 3 H), 6.22 (s, 1 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 11.6, 90.6, 112.2, 149.5, 152.0, 163.5.

Anal. Calcd for $C_6H_4Br_2O_2$: C, 26.90; H, 1.50; Br, 59.65. Found: C, 27.10; H, 1.44; Br, 59.67.

3-Butylidene-1-(4-tolyl)pyrrolidine-2,5-dione (8)

A soln of *N*-(4-tolyl)maleimide (**7**, 2.00 g, 10.70 mmol) and Ph_3P (2.80 g, 10.70 mmol) in THF (50 mL) was stirred at r.t. for 30 min. To the mixture was added butyraldehyde (1.16 g, 16.04 mmol) and it was gently refluxed for 10 h. The THF was removed in vacuo at 50 °C and the residue was purified by column chromatography (silica gel, PE–EtOAc, 9:1) to give **8** (2.34 g, 90%); as a colorless solid; mp 90–92 °C (PE–EtOAc).

IR (Nujol): 1773, 1709, 1676 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.99 (t, *J* = 8 Hz, 3 H), 1.58 (sextet, *J* = 8 Hz, 2 H), 2.23 (q, *J* = 8 Hz, 2 H), 2.39 (s, 3 H), 3.39 (s, 2 H), 6.95 (t, *J* = 8 Hz, 1 H), 7.20 (d, *J* = 8 Hz, 2 H), 7.29 (d, *J* = 8 Hz, 2 H).

MS: *m*/*z* = 243, 228, 214, 133, 95, 67, 53.

Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04; N, 5.76. Found: C, 73.92; H, 7.15; N, 5.69.

3-(4-Tolylcarbamoyl)hept-3-enoic Acid (9)

To a soln of **8** (2.00 g, 8.23 mmol) in THF (25 mL) was added aq 2 M LiOH (4 mL) in a dropwise fashion at 0 °C and the mixture was

stirred at r.t. for 5 h. THF was removed in vacuo and the aqueous layer was acidified with aq 2 M HCl till pH 4 and extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with H_2O and brine and dried (Na_2SO_4). Concentration of the organic layer in vacuo gave **9** (1.99 g, 93%) as a colorless solid; mp 140–142 °C (PE–EtOAc).

IR (Nujol): 3283, 1682, 1657, 1597 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 0.94 (t, *J* = 6 Hz, 3 H), 1.50 (sextet, *J* = 8 Hz, 2 H), 2.31 (s, 3 H), 2.15–2.40 (m, 2 H), 3.39 (s, 2 H), 6.46 (t, *J* = 6 Hz, 1 H), 7.13 (d, *J* = 8 Hz, 2 H), 7.40 (d, *J* = 8 Hz, 2 H), 8.07 (br s, 1 H).

Anal. Calcd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found: C, 68.89; H, 7.40; N, 5.28.

4-Butyl-5-(4-tolylimino)furan-2(5*H*)-one (10)

To a slurry of **9** (1.50 g, 5.75 mmol) in CH_2Cl_2 (25 mL) was added Et_3N (2.40 mL, 17.24 mmol) in a dropwise fashion with constant stirring at 0 °C. To the resulting mixture was added a soln of cyanuric chloride (1.16 g, 6.22 mmol) in CH_2Cl_2 (25 mL) and the mixture was further stirred under an argon atmosphere at r.t. for 8 h. The mixture was concentrated in vacuo and the residue was dissolved in EtOAc (50 mL). The organic layer was washed with H_2O, 5% aq $NaHCO_3$, brine, and dried (Na_2SO_4). The EtOAc layer was concentrated in vacuo and the crude product was purified by column chromatography (silica gel, PE–EtOAc, 9:1) to give pure **10** (1.19 g, 85%) as a yellowish thick oil.

IR (neat): 1798, 1682, 1622 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 0.99 (t, *J* = 8 Hz, 3 H), 1.46 (sextet, *J* = 8 Hz, 2 H), 1.70 (quintet, *J* = 8 Hz, 2 H), 2.37 (s, 3 H), 2.67 (dt, *J* = 8, 2 Hz, 2 H), 6.31 (t, *J* = 2 Hz, 1 H), 7.19 (d, *J* = 8 Hz, 2 H), 7.35 (d, *J* = 8 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.6, 20.9, 22.2, 25.8, 29.3, 120.9, 125.2, 129.3, 137.0, 140.9, 150.0, 159.6, 167.0.

Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04; N, 5.76. Found: C, 73.88; H, 7.15; N, 5.67.

2-Butylmaleic Acid (11)

A soln of **10** (1.00 g, 4.12 mmol) in glacial AcOH–concd HCl (1:1, 20 mL) was refluxed for 66 h. The mixture was allowed to reach r.t., concentrated in vacuo, and the thus obtained residue was dissolved in 5% aq $NaHCO_3$ (40 mL). The aqueous layer was washed with EtOAc (2 × 50 mL). The aqueous layer was acidified with aq 2 M HCl till pH 4 and then extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with H_2O and brine and dried (Na_2SO_4). Concentration of the organic layer in vacuo gave **11** (680 mg, 96%) as a colorless solid; mp 163–164 °C (PE–EtOAc).

IR (Nujol): 2700–2500, 1690, 1647 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$/DMSO-d_6): δ = 0.94 (t, *J* = 8 Hz, 3 H), 1.48 (sextet, *J* = 8 Hz, 2 H), 2.17 (q, *J* = 8 Hz, 2 H), 2.56–2.63 (m, 2 H), 6.90 (t, *J* = 8 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$/DMSO-d_6): δ = 12.6, 20.5, 29.5, 31.0, 125.5, 143.4, 167.5, 171.4.

Anal. Calcd for $C_8H_{12}O_4$: C, 55.81; H, 7.02. Found: C, 55.74; H, 7.13.

3-Butylfuran-2,5-dione (12)

A soln of **11** (600 mg, 3.49 mmol) in Ac_2O (15 mL) was heated at 60 °C for 3 h. The mixture was concentrated under vacuum to give a crude residue that on careful column chromatography (silica gel, PE–EtOAc, 9:1) gave pure **12** (480 mg, 90%) as a yellowish thick oil.

IR ($CHCl_3$): 1844, 1773, 1638 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 0.96 (t, *J* = 8 Hz, 3 H), 1.42 (sextet, *J* = 8 Hz, 2 H), 1.64 (quintet, *J* = 8 Hz, 2 H), 2.54 (dt, *J* = 8, 2 Hz, 2 H), 6.60 (t, *J* = 2 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.6, 22.2, 25.6, 28.9, 128.4, 153.8, 164.0, 165.9.

Anal. Calcd for $C_8H_{10}O_3$: C, 62.33; H, 6.54. Found: C, 62.40; H, 6.47.

3-Butyl-5-hydroxy-5-methylfuran-2(5*H*)-one (13a) and 4-Butyl-5-hydroxy-5-methylfuran-2(5*H*)-one (13b)

Obtained by using the typical procedure for **4a** and **4b** in 62% and 9% yield, respectively.

13a

Yellowish thick oil.

IR ($CHCl_3$): 3462, 1755, 1609 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 0.94 (t, *J* = 8 Hz, 3 H), 1.28–1.60 (m, 4 H), 1.70 (s, 3 H), 2.28 (dt, *J* = 8, 2 Hz, 2 H), 3.26 (br s, 1 H), 6.82 (t, *J* = 2 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.7, 22.3, 24.6, 24.9, 29.3, 104.1, 136.4, 146.5, 171.2.

Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.61; H, 8.32.

13b

Yellowish thick oil.

IR ($CHCl_3$): 3381, 1744, 1670 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 0.94 (t, *J* = 8 Hz, 3 H), 1.30–1.50 (m, 2 H), 1.50–1.70 (m, 2 H), 1.63 (s, 3 H), 2.20–2.45 (m, 2 H), 5.71 (t, *J* = 2 Hz, 1 H).

Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.56; H, 8.07.

3-Butyl-5-methylenefuran-2(5*H*)-one (14a)

Obtained using the typical procedure for **5a** in 90% yield as a yellowish thick oil.

IR ($CHCl_3$): 1773, 1655 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 0.94 (t, *J* = 8 Hz, 3 H), 1.37 (sextet, *J* = 8 Hz, 2 H), 1.50–1.66 (m, 2 H), 2.38 (t, *J* = 8 Hz, 2 H), 4.77 (d, *J* = 2 Hz, 1 H), 5.11 (d, *J* = 2 Hz, 1 H), 7.03 (t, *J* = 2 Hz, 1 H).

Anal. Calcd for $C_9H_{12}O_2$: C, 71.03; H, 7.94. Found: C, 70.92; H, 7.89.

4-Butyl-5-methylenefuran-2(5*H*)-one (14b)

Obtained using the typical procedure for **5a** in 87% yield as a yellowish thick oil.

IR ($CHCl_3$): 1773, 1657 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 0.96 (t, *J* = 8 Hz, 3 H), 1.42 (sextet, *J* = 8 Hz, 2 H), 1.63 (quintet, *J* = 8 Hz, 2 H), 2.49 (dt, *J* = 8, 2 Hz, 2 H), 4.93 (dd, *J* = 3, 2 Hz, 1 H), 5.16 (dd, *J* = 2, 2 Hz, 1 H), 5.99 (t, *J* = 2 Hz, 1 H).

Anal. Calcd for $C_9H_{12}O_2$: C, 71.03; H, 7.94. Found: C, 70.91; H, 7.88.

(*Z*)-4-Bromo-5-(bromomethylene)-3-butylfuran-2(5*H*)-one (1a) and 4-Bromo-3-butyl-5-(dibromomethylene)furan-2(5*H*)-one (1b)

Obtained using the typical procedure for **6**, the bromination of **14a** (70 mg, 0.46 mmol) with Br_2 (162 mg, 1.01 mmol). Purification was by filtration through a column of silica gel and this was followed by HPLC separation[1c] to give **1a** (53 mg, 37%) and **1b** (32 mg, 18%). Similarly, the use of 3.30 equivalents of bromine furnished **1a** (21

mg, 15%) and **1b** (73 mg, 41%). The analytical and spectral data obtained for **1a** and **1b** were in complete agreement with the reported data.[3–6]

1a
Pale yellow oil.

IR (neat): 1790, 1621 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 0.92 (t, *J* = 7 Hz, 3 H), 1.26–1.42 (m, 2 H), 1.49–1.65 (m, 2 H), 2.39 (t, *J* = 7 Hz, 2 H), 6.25 (s, 1 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 13.5, 22.4, 29.2, 25.1, 91.0, 149.9, 130.1, 133.9, 166.2.

Anal. Calcd for $C_9H_{10}Br_2O_2$: C, 34.87; H, 3.25; Br, 51.55. Found: C, 34.72; H, 3.19; Br, 51.42.

1b
Pale yellow oil.

IR (neat): 1780, 1622 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.93 (t, *J* = 7 Hz, 3 H), 1.29–1.45 (m, 2 H), 1.50–1.64 (m, 2 H), 2.40 (t, *J* = 7 Hz, 2 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 13.6, 22.2, 25.9, 28.8, 81.5, 128.3, 138.1, 144.7, 164.9.

Anal. Calcd for $C_9H_9Br_3O_2$: C, 27.80; H, 2.33; Br, 61.64. Found: C, 27.73; H, 2.41; Br, 61.50.

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