Synthesis of cyclopent-2-enones from furans using a nebulizer-based continuous flow photoreactor

Georgios I. Ioannou, Tamsyn Montagnon, Dimitris Kalaitzakis, Spiros A. Pergantis and Georgios Vassilikogiannakis*

Department of Chemistry, University of Crete, Vasilika Vouton, 71003 Iraklion, Crete, Greece
E-mail: vasil@uoc.gr

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Part A: Reactor Set-up

Figure 1. Schematic representation of NebPhotOX reactor.

Figure 2. NebPhotOX in action.
Figure 3. NebPhotOX in action.

Figure 4. The cone angle of the nebulizer.
Figure 5. The aerosol "cloud" formed after 10 sec of nebulization.

Figure 6. The aerosol "cloud" formed after 20 sec of nebulization.
SAFETY CAUTION: Measures were taken to eliminate all possible ignition sources from the fumehood area (sparks or flames, e.g. the electricity transformer for the LEDs was kept outside of the fumehood) in which the NebPhotOX system was operated. This included operating the reactor at room temperature and pressure conditions without any significant heat input from the low power LEDs used. In addition, the fumehood was always adequately ventilated with a high air flow. System operating conditions prevented oxygen stagnation in the system. Additional cautions included that the operator wears safety glasses with side shields and flame resistant safety clothing. For the fast reduction of the initially formed hydroperoxides of type A and B (Scheme 1), the two cooled collection flasks placed in series were prefilled with excess of Me₂S in MeOH (3 equiv in the first flask and 1 equiv in the second flask). Even higher excesses of the reducing agent can be used.
Part B: Experimental procedures

**Known compounds.** The following compounds were prepared as previously reported: 1a, 1b, 1f.

![Synthesis of 2-(4-fluorobenzyl)-5-methylfuran (1c)](image)

To a solution of 2-methylfuran (4.1 mL, 45 mmol) in anhydrous THF (20 mL), at 0 °C and under argon atmosphere, was added a solution of n-BuLi (12.2 mL, 1.6 M in hexanes, 19.5 mmol). The solution was stirred for 30 min at the same temperature and subsequently 1-(bromomethyl)-4-fluorobenzene (1.87 mL, 15 mmol) was added. The reaction solution was warmed to room temperature and stirred for a further 2 hours. The reaction was quenched with a saturated solution of NH₄Cl (20 mL) and the resulting mixture extracted with Et₂O (30 mL). The organic layer was separated and dried over MgSO₄ and concentrated *in vacuo*. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 100:1). Yield 95% (2.71 g).

**Synthesis of 2-benzyl-5-(pent-4-en-1-yl)furan (1d)**

To a solution of 2-benzylfuran (1a, 2.98 g, 18.83 mmol) in anhydrous THF (14 mL), at 0 °C and under argon atmosphere, was added a solution of n-BuLi (11.8 mL, 1.6 M in hexanes, 18.83 mmol). The solution was stirred for 30 min at the same temperature and subsequently 5-bromopent-1-ene (2.0 mL, 16.94 mmol) was added. The reaction solution was warmed to room temperature and stirred for a further 12 hours. The reaction was quenched with a saturated solution of NH₄Cl (20 mL) and the resulting mixture extracted with Et₂O (30 mL). The organic layer was separated, dried over MgSO₄ and concentrated *in vacuo*. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 100:1). Yield 94% (3.6 g).

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1H NMR (500 MHz, CHCl₃): δ = 7.30 (m, 2H), 7.21 (m, 3H), 5.87 (d, J=3.0 Hz, 1H), 5.85 (d, J=3.0 Hz, 1H), 5.80 (m, 1H), 5.01 (dq, J₁=17.1 Hz, J₂=1.6 Hz, 1H), 4.96 (m, 1H), 3.92 (s, 2H), 2.58 (t, J=7.6 Hz, 2H), 2.09 (q, J=7.2 Hz, 2H), 1.71 (quin, J=7.5 Hz, 2H) ppm; 13C NMR (125 MHz, CDCl₃): δ = 155.0, 152.6, 138.5, 138.3, 128.6 (2C), 128.4 (2C), 126.3, 114.8, 106.6, 105.3, 34.5, 33.1, 27.4, 27.2 ppm.

Synthesis of 2-hexyl-5-methylfuran (1e)
To a solution of 2-methylfuran (2.57 mL, 28.5 mmol) in anhydrous THF (14 mL), at 0 °C and under argon atmosphere, was added a solution of n-BuLi (7.72 mL, 1.6 M in hexanes, 12.35 mmol). The solution was stirred for 30 min at the same temperature and subsequently a solution of 1-iodohexane (1.40 mL, 9.5 mmol) in anhydrous THF (5 mL) was added. The reaction solution was warmed to room temperature and stirred for a further 2 hours. The reaction was quenched with a saturated solution of NH₄Cl (20 mL) and the resulting mixture was extracted with Et₂O (30 mL). The organic layer was separated, dried over MgSO₄ and concentrated in vacuo. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 100:1). Yield 95% (1.5 g).

1H NMR (500 MHz, CDCl₃): δ = 5.84 (s, 2H), 2.56 (t, J=7.6 Hz, 2H), 2.26 (s, 3H), 1.61 (quin, J=7.4 Hz, 2H), 1.38-1.28 (m, 6H), 0.89 (t, J=6.9 Hz, 3H) ppm; 13C NMR (125 MHz, CDCl₃): δ = 154.8, 149.9, 105.7, 105.0, 31.6, 28.9, 28.1 (2C), 22.6, 14.0, 13.5 ppm.

Synthesis of ethyl 2-(5-hexylfuran-2-yl)acetate (1g)
To a solution of 2-hexylfuran⁴ (2.59 g, 17.0 mmol) in high purity DMSO (120 mL) was added ethyl iodoacetate (2.0 mL, 17.0 mmol). Then FeSO₄•7H₂O (2.36 g, 8.5 mmol) and a solution of H₂O₂ 30% wt. (8.7 mL, 85 mmol) were added in four equal portions every 30 min, while the reaction flask was placed in a water bath at rt. The mixture was stirred at rt for a further 12 hours. Afterwards, a saturated aqueous solution of NaCl (20 mL) was added and the resulting mixture was extracted with Et₂O (3× 40 mL). The combined organic layers were washed with H₂O (2× 60 mL), dried over MgSO₄ and concentrated in vacuo. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 40:1). Yield 54% (2.18 g).

1H NMR (500 MHz, CDCl₃): δ = 6.09 (d, J=3.0 Hz, 1H), 5.90 (d, J=3.0 Hz, 1H), 4.17 (q, J=7.1 Hz, 2H), 3.62 (s, 2H), 2.57 (t, J=7.6 Hz, 2H), 1.60 (quin, J=7.5 Hz, 2H) 1.36-1.22 (m, 6H), 1.26 (t, J=7.1 Hz, 3H), 0.88 (t, J=6.8 Hz, 3H) ppm; 13C NMR (125 MHz, CDCl₃): δ = 155.0, 152.6, 138.5, 138.3, 128.6 (2C), 128.4 (2C), 126.3, 114.8, 106.6, 105.3, 34.5, 33.1, 27.4, 27.2 ppm.

MHz, CDCl₃): δ = 169.7, 156.1, 145.6, 108.3, 105.4, 61.0, 34.2, 31.5, 28.8, 28.0, 27.9, 22.5, 14.1, 14.0 ppm.

**General procedure for the preparation of 4-hydroxy-cyclopent-2-enones of type 2**

![Chemical structure](image)

1a: R¹=H, R²=Ph
1b: R¹=Me, R²=Ph
1c: R¹=Me, R²=3-F-Ph
1d: R¹=pent-4-enyl, R²=Ph
1f: R¹=Me, R²=CO₂Et
1g: R¹=tol, R²=CO₂Et

Substituted furans 1a-d and 1f-g (2.5 mmol for 1a or 5.0 mmol for 1b-d and 1f-g) and rose Bengal (1 mol%, 25.4 mg in case of 1a or 50.8 mg in case of 1b-d and 1f-g) were dissolved in MeOH (total volume 5 mL, 0.5 M for 1a or 1.0 M for 1b-d and 1f-g). The resulting solution was transferred to the nebulizer via a liquid pump (flow rate set at 0.5 mL/min) and timing was initiated for calculation of the exact flow rate. The solution was dispersed by the nebulizer into the reaction cylinder irradiated by the LEDs (natural white light 3800 - 4200 K, 10 W/m, 1050 Lm/m) using oxygen as the nebulizing gas (50 psi backpressure). When all the solution had been dispersed the exact flow rate was calculated and the three-way valve on the uptake line was switched to pure MeOH (2 mL) to flush out the system. The crude mixture was collected in the two cooled spherical flasks placed in series. A small sample of the crude mixture was concentrated in vacuo for the measurement of the conversions by ¹H NMR. Then, Me₂S (4 equiv, 730 μL, 10 mmol in case of 1a or 1.46 mL, 20 mmol in case of 1b-d and 1f-g) was added and the solution was stirred for 1 h at rt. In many cases for the rapid reduction of hydroperoxide intermediates, the two cooled collection flasks were prefilled with excess of Me₂S in MeOH (see below). When the reduction was completed, as indicated by tlc, Et₃N (0.3 equiv, 105 μL, 0.75 mmol in case of 1a or 209 μL, 1.5 mmol in case of 1b-d and 1f-g) was added and the mixture was stirred for 0.5 - 1 h at the same temperature. After completion of the reaction, a saturated aqueous solution of NH₄Cl (20 mL) was added and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were dried over MgSO₄ and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc) to afford the corresponding 4-hydroxy-cyclopent-2-enones of type 2.

For furan 1b the same protocol was applied on a larger scale (50 mmol) with very similar results. The two cooled collection flasks placed in series were prefilled with excess of Me₂S in MeOH (3 equiv in the first flask and 1 equiv in the second flask), for the fast reduction of the initially formed hydroperoxides of type A and B (Scheme 1).
4-Hydroxy-5-phenylcyclopent-2-enone (2a)$^{2,5}$

The reaction was accomplished according to the general experimental procedure described above, utilizing furan 1a (395 mg, 2.5 mmol). Consumption of the 5 mL reaction solution took 8.45 min (actual flow rate = 0.59 mL/min). Then Me$_2$S was added followed later, after completion of the reduction (as indicated by tlc), by Et$_3$N and the resulting solution was stirred at rt for a further 1 h. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 3:1). Yield 76% (330 mg).

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 7.64 (dd, $J_1$=5.8 Hz, $J_2$=2.2 Hz, 1H), 7.36 (m, 2H), 7.30 (m, 1H), 7.15 (m, 2H), 6.36 (dd, $J_1$=5.8 Hz, $J_2$=1.3 Hz, 1H), 5.02 (m, 1H), 3.47 (d, $J$=2.9 Hz, 1H), 2.24 (d, $J$=6.1 Hz, 1H) ppm; $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 206.4, 163.1, 136.5, 133.1, 128.4 (2C), 127.9 (2C), 78.0, 61.3 ppm.

The relative configuration was assigned by comparing the reported NMR data from the literature$^{2,5}$ with our data.

4-Hydroxy-4-methyl-5-phenylcyclopent-2-enone (2b)$^{2,6}$

The reaction was accomplished according to the general experimental procedure described above, utilizing furan 1b (860 mg, 5.0 mmol). Consumption of the 5 mL reaction solution took 9.20 min (actual flow rate = 0.54 mL/min). Then Me$_2$S was added followed later, after completion of the reduction (as indicated by tlc), by Et$_3$N and the solution stirred at rt for a further 1h. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 4:1). Yield 70% (658 mg).

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 7.51 (d, $J$=5.8 Hz, 1H), 7.35 (m, 2H), 7.30 (m, 1H), 7.12 (m, 2H), 6.29 (d, $J$=5.8 Hz, 1H), 3.82 (s, 1H), 2.02 (brs, 1H), 1.07 (s, 3H) ppm; $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 206.1, 165.6, 135.2, 132.2, 129.8 (2C), 126.9, 80.3, 65.5, 25.7 ppm.

The relative configuration was assigned by comparing the reported NMR data from the literature$^{2,6}$ with our data.

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5-(4-Fluorophenyl)-4-hydroxy-4-methylcyclopent-2-enone (2c)
The reaction was accomplished according to the general experimental procedure
described above, utilizing furan 1c (950 mg, 5.0 mmol). Consumption of the 5 mL
reaction solution took 8.95 min (actual flow rate = 0.56 mL/min). Then Me₂S was
added followed later, after completion of the reduction (as indicated by tlc), by Et₃N
and the resulting solution stirred at rt for a further 1h. The product was purified by
flash column chromatography (silica gel, petroleum ether:EtOAc = 3:1). Yield 76%
(784 mg).

¹H NMR (500 MHz, CDCl₃): δ = 7.49 (d, J=5.9 Hz, 1H), 7.10-7.02 (m, 4H), 6.25 (d,
J=5.9 Hz, 1H), 3.79 (s, 1H), 2.37 (brs, 1H), 1.03 (s, 3H) ppm; ¹³C NMR (125 MHz,
CDCl₃): δ = 205.8, 165.7, 162.1 (d, J=246.1 Hz, F-Ph-C(ipso)), 132.0, 131.3 (d, J=8.0
Hz, F-Ph-C(meta), 2C), 130.9 (d, J=3.2 Hz, F-Ph-C(para)), 115.5 (d, J=21.3 Hz, F-
Ph-C(ortho), 2C), 80.1, 64.7, 25.7 ppm; HRMS (TOF ESI): calcd for C₁₂H₁₂FO₂:
207.0816 [M+H]+; found: 207.0816.

NOE
The relative configuration gives an upfield shift of the signal for
the methyl group (1.03 ppm) as a result of the shielding effect
from the aromatic ring when these two groups are cis
configured.⁶a

4-Hydroxy-4-(pent-4-enyl)-5-phenylcyclopent-2-enone (2d)
The reaction was accomplished according to the general experimental procedure
described above, utilizing furan 1d (1.13 g, 5.0 mmol). Consumption of the 5 mL
reaction solution took 9.83 min (actual flow rate = 0.51 mL/min). Then Me₂S was
added followed later, after completion of the reduction (as indicated by tlc), by Et₃N
and the resulting solutions stirred at rt for a further 1h. The product was purified by
flash column chromatography (silica gel, petroleum ether:EtOAc = 8:1). Yield 67%
(811 mg).

¹H NMR (500 MHz, CDCl₃): δ = 7.55 (d, J=5.9 Hz, 1H), 7.35 (m, 2H), 7.30 (m, 1H),
7.16 (m, 2H), 6.33 (d, J=5.9 Hz, 1H), 5.58 (m, 1H), 4.86 (m, 2H), 3.84 (s, 1H), 2.08
(brs, 1H), 1.82 (m, 2H), 1.40-1.23 (m, 4H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ =
205.4, 164.1, 137.8, 134.5, 132.9, 129.9 (2C), 128.4 (2C), 127.4, 114.9, 82.5, 66.0,
38.5, 33.7, 23.0 ppm; HRMS (TOF ESI): calcd for C₁₆H₁₉O₂: 243.1380 [M+H]+;
found: 243.1371.
Ethyl 2-hydroxy-2-methyl-5-oxocyclopent-3-enecarboxylate (2f)<sup>2</sup>

The reaction was accomplished according to the general experimental procedure described above, utilizing furan 1f (840 mg, 5.0 mmol). Consumption of the 5 mL reaction solution took 10.27 min (actual flow rate = 0.49 mL/min). Then Me<sub>2</sub>S was added followed later, after completion of the reduction (as indicated by tlc), by Et<sub>3</sub>N and the resulting solution stirred at rt for a further 0.5 h. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 2:1). Yield 61% (561 mg). The diastereomeric ratio of the easily epimerizable product 2f was determined as being 5:1 in the crude reaction mixture and 2:1 after the chromatographic purification.

For this substrate (1f), the procedure was repeated a number of times using air as the nebulizing gas for different initial substrate concentrations (Table 2 in main text of paper). These latter experiments were conducted with the pyrex reaction chamber placed in a vertical position. Exact flow rates were between 0.55 – 0.62 mL/min and isolated yields varied from 48 – 69 % (see, Table 2). In all other aspects these procedures were identical to the one described above.

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ = 7.49 (d, J=5.7 Hz, 1H for major), 7.42 (d, J=5.7 Hz, 1H for minor), 6.12 (d, J=5.7 Hz, 1H for minor plus 1H for major), 4.20 (m, 2H for major plus 2H for minor), 3.78 (s, 1H for major), 3.64 (s, 1H for minor), 3.38 (s, 1H for major), 1.53 (s, 3H for major), 1.48 (s, 3H for minor), 1.28 (t, J=7.2 Hz, 3H for major), 1.26 (t, J=7.2 Hz, 3H for minor) ppm; <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ = 201.0 (minor), 200.1 (major), 168.3 (1C for major plus 1C minor), 167.5 (major), 165.9 (minor), 131.8 (1C for major plus 1C minor), 78.8 (minor), 77.2 (major), 64.3 (minor), 62.4 (major), 62.0 (major), 61.3 (minor), 27.4 (major), 23.9 (minor), 14.1 (minor), 14.0 (major) ppm.

The relative configuration was assigned by comparing the reported NMR data from the literature.<sup>2</sup>
Ethyl 2-hexyl-2-hydroxy-5-oxocyclopent-3-ene carboxylate (2g)

The reaction was accomplished according to the general experimental procedure described above, utilizing furan 1g (1.19 g, 5.0 mmol). Consumption of the 5 mL reaction solution took 10.90 min (actual flow rate = 0.46 mL/min). Then Me2S was added followed later, after completion of the reduction (as indicated by tlc), by Et3N and the resulting solution stirred at rt for a further 1h. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 2:1). Yield 47% (597 mg). The diastereomeric ratio of the easily epimerizable product 2g was determined as being 3:1 in the crude reaction mixture and 13:1 after the chromatographic purification.

1H NMR (500 MHz, CDCl3): δ = 7.51 (d, J=5.7 Hz, 1H), 6.18 (d, J=5.7 Hz, 1H), 4.24 (q, J=7.1 Hz, 2H), 3.70 (s, 1H), 3.44 (s, 1H), 1.81 (m, 1H), 1.69 (m, 1H), 1.43-1.24 (m, 8H), 1.31 (t, J=6.8 Hz, 3H), 0.88 (t, J=6.9 Hz, 3H) ppm; 13C NMR (125 MHz, CDCl3): δ = 200.1, 168.7, 167.2, 132.3, 79.8, 62.1, 60.9, 40.3, 31.6, 29.4, 23.8, 22.5, 14.0 (2C) ppm; HRMS (TOF ESI): calcd for C14H21O4: 253.1445 [M-H]-; found: 253.1435.

NOE

General procedure for the preparation of 4-methoxy-2-cyclopentenones of type 3

Substituted furans 1a-1g (2.5 mmol for 1a or 5.0 mmol for 1b-1g) and rose Bengal (1 mol%, 25.4 mg in case of 1a or 50.8 mg in case of 1b-1g) were dissolved in MeOH (total volume 5 mL, 0.5 M for 1a or 1.0 M for 1b-1g). The resulting solution was transferred to the nebulizer via a liquid pump (flow rate set at 0.5 mL/min) and timing was initiated for calculation of the exact flow rate. The solution was dispersed by the nebulizer into the reaction cylinder irradiated by the LEDs (natural white light 3800 - 4200 K, 10 W/m, 1050 Lm/m) using oxygen as the nebulizing gas (50 psi backpressure). When all the solution had been dispersed the exact flow rate was calculated and the three-way valve on the uptake line was switched to pure MeOH (2
mL) to flush out the system. The flow rate was measured based on the time needed for the nebulization of 5 mL of photooxidation solution. The crude solution was collected in the two cooled spherical flasks placed in series. A small sample of the crude solution was concentrated in vacuo for the measurement of the conversion by $^1$H NMR. Then, Me$_2$S (4.0 equiv, 730 μL, 10 mmol in case of 1a or 1.46 mL, 20 mmol in case of 1b-1g) was added and the solution was stirred for 1 h at rt. In many cases for the rapid reduction of hydroperoxide intermediates, the two cooled collection flasks were prefilled with excess of Me$_2$S in MeOH. When the reduction was completed, as indicated by tlc, Et$_3$N (0.5 equiv, 348 μL, 2.5 mmol in case of 1b-1d and 1f, or 174 μL, 1.25 mmol in case of 1a or 1.0 equiv, 696 μL, 5.0 mmol in case of 1g) or NaOH (1.5 equiv, 300 mg, 7.5 mmol in case of 1e) was added and the solution was stirred for 1 - 12 h at the same temperature. After the completion of the reaction, a saturated aqueous solution of NH$_4$Cl (20 mL) was added and the mixture was extracted with EtOAc (3× 20 mL). The combined organic layers were dried over MgSO$_4$ and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc) to afford the corresponding 4-methoxy-cyclopent-2-enones of type 3.

4-Methoxy-2-phenylcyclopent-2-enone (3a)

The reaction was accomplished according to the general experimental procedure described above, utilizing furan 1a (395 mg, 2.5 mmol). Consumption of the 5 mL reaction solution took 9.15 min (actual flow rate = 0.55 mL/min). Then Me$_2$S was added followed later, after completion of the reduction (as indicated by tlc), by Et$_3$N and the resulting solution stirred at rt for further 12 h. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 6:1). Yield 65% (306 mg).

$^1$H NMR (500 MHz, CDCl$_3$): $\delta = 7.70$ (m, 3H), 7.39 (m, 3H), 4.62 (dt, $J_1=5.9$ Hz, $J_2=2.4$ Hz, 1H), 3.48 (s, 3H), 2.91 (dd, $J_1=18.3$ Hz, $J_2=5.9$ Hz, 1H), 2.54 (dd, $J_1=18.2$ Hz, $J_2=2.3$ Hz, 1H) ppm; $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta = 203.4$, 154.0, 144.5, 130.4, 128.9, 128.3 (2C), 127.4 (2C), 75.9, 56.8, 42.7 ppm.

4-Methoxy-3-methyl-2-phenylcyclopent-2-enone (3b)


The reaction was accomplished according to the general experimental procedure described above, utilizing furan 1b (860 mg, 5.0 mmol). Consumption of the 5 mL reaction solution took 9.25 min (actual flow rate = 0.54 mL/min). Then Me$_2$S was added followed later, after completion of the reduction (as indicated by tlc), by Et$_3$N and the resulting solution stirred at rt for further 12 h. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 6:1). Yield 75% (757 mg).

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 7.41 (m, 2H), 7.32 (m, 3H), 4.46 (m, 1H), 3.47 (s, 3H), 2.81 (dd, $J_1$=18.1 Hz, $J_2$=5.9 Hz, 1H), 2.49 (dd, $J_1$=18.1 Hz, $J_2$=2.1 Hz, 1H), 2.20 (s, 3H) ppm; $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 203.2, 168.2, 141.7, 130.7, 129.1 (2C), 128.2 (2C), 128.0, 79.6, 57.3, 40.9, 14.9 ppm.

2-(4-Fluorophenyl)-4-methoxy-3-methylocyclopent-2-enone (3c)

The reaction was accomplished according to the general experimental procedure described above, utilizing furan 1c (950 mg, 5.0 mmol). Consumption of the 5 mL reaction solution took 9.22 min (actual flow rate = 0.54 mL/min). Then Me$_2$S was added followed later, after completion of the reduction (as indicated by tlc), by Et$_3$N and the resulting solution stirred at rt for further 12 h. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 3:1). Yield 69% (759 mg).

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 7.30 (m, 2H), 7.10 (m, 2H), 4.46 (m, 1H), 3.47 (s, 3H), 2.80 (dd, $J_1$=18.1 Hz, $J_2$=6.0 Hz, 1H), 2.48 (dd, $J_1$=18.1 Hz, $J_2$=2.2 Hz, 1H), 2.19 (s, 3H) ppm; $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 203.1, 168.2, 162.5 (d, $J$=247.5 Hz, F-Ph-C(ipso)), 140.7, 130.9 (d, $J$=8.2 Hz, F-Ph-C(meta), 2C), 126.7 (d, $J$=3.4 Hz, F-Ph-C(para)), 115.3 (d, $J$=21.6 Hz, F-Ph-C(ortho), 2C), 79.6, 57.4, 40.9, 15.0 ppm; HRMS (TOF ESI): calcd for C$_{13}$H$_{14}$FO$_2$: 221.0972 [M+H]$^+$; found: 221.0976.

4-Methoxy-3-(pent-4-enyl)-2-phenylcyclopent-2-enone (3d)

The reaction was accomplished according to the general experimental procedure described above, utilizing furan 1d (1.13 g, 5.0 mmol). Consumption of the 5 mL reaction solution took 9.63 min (actual flow rate = 0.52 mL/min). Then Me$_2$S was added followed later, after completion of the reduction (as indicated by tlc), by Et$_3$N and the resulting solution stirred at rt for further 12 h. The product was purified by
flash column chromatography (silica gel, petroleum ether:EtOAc = 10:1). Yield 71% (909 mg).

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 7.41 (m, 2H), 7.34 (m, 1H), 7.25 (m, 2H), 5.75 (m, 1H), 4.96 (m, 2H), 4.58 (dd, $J_1$=6.0 Hz, $J_2$=2.1 Hz, 1H), 3.46 (s, 3H), 2.81 (dd, $J_1$=18.1 Hz, $J_2$=5.9 Hz, 1H), 2.48 (dd, $J_1$=18.1 Hz, $J_2$=2.2 Hz, 1H), 2.07 (m, 2H), 1.74 (m, 1H), 1.59 (m, 1H) ppm; $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 203.2, 171.6, 141.9, 137.5, 130.8, 128.9 (2C), 128.1 (2C), 127.9, 115.1, 77.4, 57.2, 40.8, 33.5, 27.6, 26.5 ppm; HRMS (TOF ESI): calcd for C$_{17}$H$_{21}$O$_2$: 257.1536 [M+H]$^+$; found: 257.1531.

2-Hexyl-4-methoxy-3-methylcyclopent-2-enone (3e)
The reaction was accomplished according to the general experimental procedure described above, utilizing furan 1e (830 mg, 5.0 mmol). Consumption of the 5 mL reaction solution took 10.58 min (actual flow rate = 0.47 mL/min). Then Me$_2$S was added followed later, after completion of the reduction (as indicated by tlc), by NaOH and the resulting solution stirred at rt for further 12 h. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 10:1). Yield 50% (490 mg).

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 4.30 (brd, $J$=5.7 Hz, 1H), 3.38 (s, 3H), 2.61 (dd, $J_1$=18.1 Hz, $J_2$=5.9 Hz, 1H), 2.26 (dd, $J_1$=18.1 Hz, $J_2$=1.7 Hz, 1H), 2.16 (m, 2H), 2.04 (s, 3H), 1.37 (m, 2H), 1.27 (m, 4H), 0.86 (t, $J$=7.0 Hz, 3H) ppm; $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 205.1, 166.8, 142.9, 79.7, 56.9, 40.5, 31.7, 27.7, 22.8, 22.4, 13.9 (2C) ppm; HRMS (TOF ESI): calcd for C$_{12}$H$_{21}$O$_2$: 197.1536 [M+H]$^+$; found: 197.1528.

Ethyl 3-methoxy-2-methyl-5-oxocyclopent-1-enecarboxylate (3f)
The reaction was accomplished according to the general experimental procedure described above, utilizing furan 1f (840 mg, 5.0 mmol). Consumption of the 5 mL reaction solution took 10.22 min (actual flow rate = 0.49 mL/min). Then Me$_2$S was added followed later, after completion of the reduction (as indicated by tlc), by Et$_3$N and the resulting solution stirred at rt for a further 1 h. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 3:1). Yield 57% (564 mg).

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 4.37 (dd, $J_1$=6.1 Hz, $J_2$=2.6 Hz, 1H), 4.32 (q, $J$=7.1 Hz, 2H), 3.43 (s, 3H), 2.74 (dd, $J_1$=18.1 Hz, $J_2$=6.1 Hz, 1H), 2.41 (dd, $J_1$=18.1 Hz,
Ethyl 2-hexyl-3-methoxy-5-oxocyclopent-1-enecarboxylate (3g)

The reaction was accomplished according to the general experimental procedure described above, utilizing furan 1g (1.19 g, 5.0 mmol). Consumption of the 5 mL reaction solution took 9.83 min (actual flow rate = 0.51 mL/min). Then Me$_2$S (1.46 mL, 20 mmol, 4.0 equiv.) was added followed later, after completion of the reduction (as indicated by tlc), by Et$_3$N (696 μL, 5 mmol, 1 equiv.) and the resulting solution stirred at rt for further 12 h. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 6:1). Yield 40% (536 mg).

$^{1}$H NMR (500 MHz, CDCl$_3$): $\delta$ = 4.46 (dd, $J_1$=6.1 Hz, $J_2$=2.6 Hz, 1H), 4.31 (q, $J$=7.1 Hz, 2H), 3.41 (s, 3H), 2.81 (ddd, $J_1$=12.7 Hz, $J_2$=9.6 Hz, $J_3$=6.5 Hz, 1H), 2.74 (dd, $J_1$=18.1 Hz, $J_2$=6.1 Hz, 1H), 2.63 (ddd, $J_1$=12.7 Hz, $J_2$=9.6 Hz, $J_3$=5.6 Hz, 1H), 2.40 (dd, $J_1$=18.1 Hz, $J_2$=2.6 Hz, 1H), 1.57 (m, 2H), 1.39-1.26 (m, 6H), 1.33 (t, $J$= 7.1 Hz, 3H), 0.88 (t, $J$ = 6.8 Hz, 3H) ppm; $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 199.2, 182.3, 162.9, 133.9, 77.6, 61.1, 57.6, 41.3, 31.4, 29.5, 29.0, 27.7, 22.5, 14.1, 14.0 ppm; HRMS (TOF ESI): calcd for C$_{15}$H$_{25}$O$_4$: 269.1747 [M+H]$^+$; found: 269.1753.

General procedure for the preparation of ethyl 4-methoxy-2-oxocyclopent-3-enecarboxylate of type 4

Substituted furans 1f or 1g (5.0 mmol) and rose Bengal (1 mol%, 50.8 mg) were dissolved in MeOH (total volume 5 mL, 1 M final concentration). The resulting solution was transferred to the nebulizer via a liquid pump (flow rate set at 0.5 mL/min) and timing was initiated for calculation of the exact flow rate. The solution was dispersed by the nebulizer into the reaction cylinder irradiated by the LEDs (natural white light 3800 - 4200 K, 10 W/m, 1050 Lm/m) using oxygen as the nebulizing gas (50 psi backpressure). When all the solution had been dispersed the exact flow rate was calculated and the three-way valve on the uptake line was switched to pure MeOH (2 mL) to flush out the system. The crude mixture was collected in the two cooled spherical flasks placed in series. A small sample of the crude mixture was concentrated in vacuo for the measurement of the conversion by $^1$H NMR. Then, Me$_2$S (4.0 equiv, 1.46 mL, 20 mmol) was added and the solution was stirred for 1 h at rt. In many cases for the rapid reduction of hydroperoxide intermediates, the two cooled collection flasks were prefilled with excess of Me$_2$S in
MeOH. When the reduction was completed as indicated by tlc, Et₃N (5.0 equiv, 3.48 mL, 25 mmol) was added and the mixture was stirred for 12 – 48 h at the same temperature. After completion of the reaction, a saturated aqueous solution of NH₄Cl (20 mL) was added and the mixture was extracted with EtOAc (3× 20 mL). The combined organic layers were dried over MgSO₄ and concentrated in vacuo. The crude mixture was purified by flash column chromatography (silica gel, petroleum ether:EtOAc) to afford the corresponding ethyl 4-methoxy-2-oxocyclopent-3-enecarboxylates of type 4.

**Ethyl 3-methoxy-2-methyl-5-oxocyclopent-3-ene-1-carboxylate (4f)**

The reaction was accomplished according to the general experimental procedure described above, utilizing furan 1f (840 mg, 5.0 mmol). Consumption of the 5 mL reaction solution took 10.18 min (actual flow rate = 0.49 mL/min). Then Me₂S was added followed later, after completion of the reduction (as indicated by tlc), by Et₃N and the resulting mixture stirred at rt for further 12 h. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 3:1). Yield 62% (614 mg).

1H NMR (500 MHz, CDCl₃): δ = 5.23 (s, 1H), 4.22 (q, J=7.1 Hz, 2H), 3.87 (s, 3H), 3.26 (qd, J₁=7.1 Hz, J₂=3.0 Hz, 1H), 3.11 (d, J=3.0 Hz, 1H), 1.30 (t, J=7.1 Hz, 3H), 1.27 (d, J=7.3 Hz, 3H) ppm; 13C NMR (125 MHz, CDCl₃): δ = 197.1, 193.3, 169.0, 101.7, 61.5, 60.2, 59.1, 39.2, 17.0, 14.1 ppm; HRMS (TOF ESI): calcd for C₁₀H₁₅O₄: 199.0965 [M+H]+; found: 199.0963.

NOE The J coupling of 3.0 Hz for the hydrogen at 3.11 ppm indicates a trans relative configuration.

**Ethyl 2-hexyl-3-methoxy-5-oxocyclopent-3-ene-1-carboxylate (4g)**

The reaction was accomplished according to the general experimental procedure described above, utilizing furan 1g (1.19 g, 5.0 mmol). Consumption of the 5 mL reaction solution took 10.68 min (actual flow rate = 0.47 mL/min). Then Me₂S was added followed later, after completion of the reduction (as indicated by tlc), by Et₃N
and the resulting mixture stirred at rt for further 48 h. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 10:1). Yield 47% (630 mg).

$^1$H NMR (500 MHz, CDCl$_3$): $\delta = 5.24$ (d, $J=0.8$ Hz, 1H), 4.22 (q, $J=7.1$ Hz, 2H), 3.86 (s, 3H), 3.20 (m, 1H), 3.17 (d, $J=3.0$ Hz, 1H), 1.83 (m, 1H), 1.38 (m, 1H), 1.29 (t, $J=7.0$ Hz, 3H), 1.26 (m, 8H), 0.88 (t, $J=6.8$ Hz, 3H) ppm; $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta = 197.4, 192.8, 169.3, 102.1, 61.4, 59.1, 58.2, 44.5, 31.5, 31.2, 28.9, 26.5, 22.4, 14.1, 13.9$ ppm; HRMS (TOF ESI): calcd for C$_{15}$H$_{25}$O$_4$: 269.1747 [M+H]$^+$; found: 269.1747.

NOE

The $J$ coupling of 3.0 Hz for the hydrogen at 3.17 ppm indicates a *trans* relative configuration.$^5$
Part C: Copies of $^1$H-NMR, $^{13}$C-NMR and NOE spectra

1c

(500 MHz, CDCl$_3$)

1c

(125 MHz, CDCl$_3$)
$^{1}H$ NMR spectra of compound 1e.

- (500 MHz, CDCl$_3$)
- (125 MHz, CDCl$_3$)
$^{1}J_{	ext{C,H}}$ (500 MHz, CDCl$_3$)

$^{1}J_{	ext{C,H}}$ (125 MHz, CDCl$_3$)
2b

(500 MHz, CDCl₃)

2b

(125 MHz, CDCl₃)
NOE experiment of compound 2c at 7.06 ppm

[Diagram showing the NOE effects and chemical shifts]

3.79 ppm
7.06 ppm
1.03 ppm
Ph

2d

(500 MHz, CDCl₃)

Ph

2d

(125 MHz, CDCl₃)
NOE experiment of compound 2d at 7.16 ppm
NOE experiment of compound 2g at 3.44 ppm
(500 MHz, CDCl₃)

(125 MHz, CDCl₃)
$\text{OPhMe}_3\text{bMe}$

($500 \text{ MHz, CDCl}_3$)

$\text{OPhMe}_3\text{bMe}$

($125 \text{ MHz, CDCl}_3$)
3d
(500 MHz, CDCl₃)

3d
(125 MHz, CDCl₃)
MeO
\[ nC_3H_11 \]
Me
3e

(500 MHz, CDCl₃)

MeO
\[ nC_3H_11 \]
Me
3e

(125 MHz, CDCl₃)
NOE experiment of compound 4f at 3.11 ppm
NOE experiment of compound 4g at 1.83 ppm