Merging singlet-oxygen induced furan oxidations with organocatalysis. Synthesis of enantiopure cyclopentanones and hydrindanes

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Part A: General methods and Experimental procedures.

General Methods:
NMR data were obtained for $^1$H at 500 MHz and for $^{13}$C at 125 MHz. HRMS data was recorded on the Orbitrap analyzer of an LTQ Orbitrap XL, using an ESI ionization source. Enantiomeric excesses were determined by HPLC (UFLC) analysis using a chiral column and in comparison with the corresponding racemates. The columns used were a Daicel Chiralpak AD-H Column (250 × 4.6 mm), a Chiralpak AS-H Column (250 × 4.6 mm) or a Chiralcel OD Column (250 × 4.6 mm). Optical rotations were measured on an automatic polarimeter P3000 (A. Krüss Optronic). $[\alpha]_D^T$ values are quoted in g/100 mL concentration using a 50 mm polarimeter tube; D refers to the D-line of sodium (589 nm); temperatures (T) are given in degrees Celsius (°C).

The organocatalyst (cat. 1), as well as, the compounds 2,5-dimethyl furan 1a, trans-cinnamaldehyde 2a, trans-4-methoxycinnamaldehyde 2b, trans-4-chlorocinnamaldehyde 2c, and trans-2-methoxycinnamaldehyde 2e are commercially available.

Synthesis of furan substrates 1b and 1c, as well as, enals 2d and 2f

\[ \text{Me} \quad \circ \quad \text{Me} \]

1b

\[ \text{Me} \quad \circ \quad \text{Me} \]

1c

The furans 1b\(^1\) and 1c\(^2\) and the enals 2d\(^3\) and 2f\(^3\) were prepared according to previously reported methodologies.

Synthesis of 2,5-diethylfuran (1d)\(^4\)

\[ \text{Et} \quad \circ \quad \text{Et} \]

1d

To a solution of 2-ethylfuran (1.05 mL, 10.0 mmol) in anhydrous THF (35 mL), at 0 °C and under an argon atmosphere, was added dropwise a solution of n-BuLi (6.25 mL, 1.6 M in hexane, 10.0 mmol). The solution was stirred for 30 min at the same temperature, and, subsequently, a solution of iodoethane (1.20 mL, 15 mmol) in anhydrous THF (3 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 aqueous solution of NH\(_4\)Cl (10 mL) and the resulting mixture was extracted.

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with Et₂O (20 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). Yield = 1.0 g (81%).

¹H NMR (500 MHz, CDCl₃): δ 5.86 (s, 2H), 2.61 (q, J = 7.5 Hz, 4H), 1.22 (t, J = 7.5 Hz, 6H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 155.9 (2C), 104.1 (2C), 21.3 (2C), 12.2 (2C) ppm.

Synthesis of enediones 1ai, 1aii and 1bi, 1bii

2,5-Disubstituted furans (0.2 mmol, 21.3 µL for 1a, 33.2 mg for 1b) were dissolved in methanol (4 mL, 50 mM) containing catalytic amounts of rose Bengal as photosensitizer (0.1 mM). The solutions were cooled using an ice bath. Oxygen was gently bubbled through the solutions while they were irradiated by a xenon Variac Eimac Cermax 300 W lamp (VIS 385-740 nm). The reactions were monitored by tlc. After completion of the reactions (3 min), the solutions were warmed to room temperature and Me₂S (58 µL, 0.8 mmol) was added. After completion of the reduction (45 min), the solutions were concentrated in vacuo and the residues were purified by flash column chromatography (silica gel, petroleum ether : EtOAc 10:1 → 4/1) to afford the corresponding cis-enediones 1ai and 1bi.

Towards to the synthesis of 1aii, after the photooxygenation reaction the solvent (MeOH) was replaced by DCM (2 mL) and Me₂S (58 µL, 0.8 mmol) was added. After completion of the reduction (1 h), p-toluenesulfonic acid (PTSA·H₂O, 3.8 mg, 0.02 mmol) was added and the solution was stirred until completion of the isomerization (1ai→1aii) was observed by ¹H-NMR after 4 h. The solvent was removed under reduced pressure and the product was purified by flash column chromatography (silica gel, petroleum ether : EtOAc 6:1 → 5/1) to afford 1aii as a white solid. Yield 80% (17.9 mg).

(Z)-Hex-3-ene-2,5-dione (1ai)

Yield = 15.7 mg (70%) of a slightly yellow oil. The Z-configuration was assigned by comparing the ¹H and ¹³C NMR data with the corresponding known literature data.

¹H NMR (500 MHz, CDCl₃): 6.28 (s, 2H), 2.27 (s, 6H) ppm; ¹³C NMR (125 MHz, CDCl₃): 200.5 (2C), 135.6 (2C), 29.7 (2C) ppm.

(Z)-Undec-3-ene-2,5-dione (1bi)

Yield = 30.9 mg (85%) of a yellow oil. The Z-configuration was assigned by the coupling constant J for the vinyl protons (J=11.9 Hz).
\(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 6.31 (d, \(J=11.9\) Hz, 1H) 6.28 (d, \(J=11.9\) Hz, 1H), 2.53 (t, \(J=7.4\) Hz, 2H), 2.29 (s, 3H), 1.62 (m, 2H), 1.32-1.25 (m, 6H), 0.87 (t, \(J=7.0\) Hz, 3H) ppm; \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) 202.8, 200.7, 136.1, 135.2, 42.6, 31.6, 29.7, 28.7, 23.4, 22.4, 14.0 ppm.

To the cis-enediones (0.1 mmol, 11.2 mg for 1ai and 18.2 mg for 1bi) in EtOH/H\(_2\)O (9:1 v/v, 1 mL) was added the organocatalyst (S)-2-(diphenyl ((trimethylsilyl) oxy)methyl) pyrrolidine (6.5 mg, 0.02 mmol, 20% mol) and the resulting solutions were stirred for 30 min until full consumption of the starting material was indicated by tlc analysis. The solvent was concentrated in vacuo and the corresponding trans-enediones 1aii and 1bii were purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 8:1 → 4:1).

(E)-Hex-3-ene-2,5-dione (1aii)

Yield = 8.7 mg (78%) of white solid. The \(E\)-configuration was assigned by comparing the \(^1\)H and the \(^{13}\)C NMR data with the corresponding known literature data.\(^4\)

\(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 6.79 (s, 2H), 2.38 (s, 6H) ppm; \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): 198.5 (2C), 137.8 (2C), 28.0 (2C) ppm.

(E)-Undec-3-ene-2,5-dione (1bii)

Yield = 14.6 mg (80%) of white solid. The \(E\)-configuration was assigned by the coupling constant \(J\) for the vinyl protons (\(J=16.6\) Hz).

\(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 6.84 (d, \(J=16.6\) Hz, 1H), 6.80 (d, \(J=16.6\) Hz, 1H), 2.63 (t, \(J=7.3\) Hz, 2H), 2.36 (s, 3H), 1.62 (m, 2H), 1.32-1.26 (m, 6H), 0.87 (t, \(J=6.8\) Hz, 3H) ppm; \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) 200.8, 198.5, 137.2, 136.8, 41.4, 31.5, 28.7, 28.1, 23.7, 22.4, 14.0 ppm.

General procedure for the organocatalysed synthesis of cyclopentanones of type 3 from 1ai

\(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 6.31 (d, \(J=11.9\) Hz, 1H) 6.28 (d, \(J=11.9\) Hz, 1H), 2.53 (t, \(J=7.4\) Hz, 2H), 2.29 (s, 3H), 1.62 (m, 2H), 1.32-1.25 (m, 6H), 0.87 (t, \(J=7.0\) Hz, 3H) ppm; \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) 202.8, 200.7, 136.1, 135.2, 42.6, 31.6, 29.7, 28.7, 23.4, 22.4, 14.0 ppm.
To a solution of enedione 1ai (11.2 mg, 0.1 mmol) in EtOH/H$_2$O (9/1 v/v, 1 mL) at room temperature, the organocatalyst (6.5 mg, 0.02 mmol, 20% mol) and the corresponding enal (0.15 mmol, 18.8 µL of 2a, or 24.3 mg of 2b, or 25 mg of 2c, or 24 mg of 2d, or 24.3 mg of 2e, or 22.5 mg of 2f) were added and the resulting solution stirred for 24 h at the same temperature. After completion of the reaction (as indicated by tlc analysis), the solution was concentrated in vacuo and the products of type 3 were purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 5:1 → 2:1 for all the products). Isolated yields: for 3a = 22 mg (90%), for 3b = 23 mg (84%), for 3c = 22 mg (79%), for 3d = 24 mg (88%), for 3e = 26 mg (95%) and for 3f = 23.6 mg (90%). All the dr values were calculated using the $^1$H-NMR data of the crude reaction mixtures. Identical results were obtained when the reactions started from 1aii.

Racemic mixtures of all the compounds of type 3 were prepared according to the general experimental procedure described above, in this case, using an equimolar mixture of (S)-(−)-α,α-diphenyl-2-pyrrolidinemethanol trimethylsilyl ether (3.2 mg, 0.01 mmol) and (R)-(−)-α,α-diphenyl-2-pyrrolidinemethanol trimethylsilyl ether (3.2 mg, 0.01 mmol) as organocatalyst.

**General procedure for the one pot synthesis of cyclopentanones of type 3 from furan 1a**

2,5-Dimethyl furan 1a (10.7 µL, 0.1 mmol) was dissolved in methanol (2 mL, 50 mM) containing catalytic amounts of rose Bengal as photosensitizer (0.1 mM). The solution was cooled using an ice bath. Oxygen was gently bubbled through the solution while it was irradiated by a xenon Variac Eimac Cermax 300 W lamp (VIS 385-740 nm) for 2 min. Then the solution was warmed to room temperature and Me$_2$S (29 µL, 0.4 mmol) was added. After tlc analysis indicated completion of the reduction (45 min), the solvent was replaced by EtOH/H$_2$O (9/1 v/v, 1 mL). Then, the organocatalyst (6.5 mg, 0.02 mmol, 20 mol%) and the corresponding enal (0.15 mmol, 18.8 µL of 2a, or 24.3 mg of 2b, or 25 mg of 2c, or 24 mg of 2d, or 24.3 mg of 2e, or 22.5 mg of 2f) were added and the solution was stirred for 24 h at room temperature. After completion of the reaction (as indicated by $^1$H-NMR of the crude reaction mixture), the solvent was concentrated in vacuo and the products of type 3 were purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 5:1 → 2:1 for all the products). All the dr values were calculated using the $^1$H-NMR of the crude reaction mixture.

When the same protocol was scaled up to 1 mmol of furan 1a with enal 2a or 2c (1.5 mmol) the results were identical.
In order to analyze the compounds by chiral HPLC and determine the ee values, the aldehyde group in products of type 3 was reduced using NaBH₄, because the two enantiomers of 3 were inseparable by chiral HPLC. The reductions were performed as follows: To each solution of pure compound of type 3 (0.06 mmol, 14.6 mg for 3a, 16.4 mg for 3b, 16.6 mg for 3c, 16.3 mg for 3d, 16.4 mg for 3e and 15.7 mg for 3f) in dry MeOH (2 mL) at 0 °C, a solution of NaBH₄ (0.7 mg, 0.0185 mmol) in dry MeOH (0.5 mL) was added dropwise. The resulting solution was stirred at the same temperature for 20 min. The reaction was then quenched by the addition of a saturated aqueous solution of NH₄Cl (1 mL) and the mixture was extracted with EtOAc (3× 3 mL). The combined organic phases were dried over MgSO₄, filtered and concentrated in vacuo. The reduced products were purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 5:1 → 1:1 for all the products). This reduction was performed to all the compounds of type 3, derived either from pure enedione 1ai or furan 1a and the ee values were identical.

(1R,2S,5S)-3-oxo-2-(2-oxopropyl)-5-phenylcyclopentane-1-carbaldehyde (3a)
Yield = 15.9 mg (65%) of a yellow oil.

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46.1, 45.8, 41.9, 41.8, 29.7 ppm; \([\alpha]_D^{20}=+40\) (c 0.5, MeOH); HRMS (Orbitrap ESI): calcd for C_{16}H_{10}O_4: 275.1278 [M+H]^+; found 275.1278.

**(1R,2S,5S)-5-(4-chlorophenyl)-3-oxo-2-(2-oxopropyl)cyclopentane-1-carbaldehyde (3c)**

Yield = 16.4 mg (59%) of a yellow oil.

\(^1H\) NMR (500 MHz, CDCl\(_3\)): 9.64 (d, J=2.2 Hz, 1H), 7.34 (d, J=8.6 Hz, 2H), 7.30 (d, J=8.6 Hz, 2H), 3.45 (td, J\(_1=11.6\) Hz, J\(_2=8.4\) Hz, 1H), 3.25 (td, J\(_1=11.2\) Hz, J\(_2=2.2\) Hz, 1H), 3.07 (dd, J\(_1=19.1\) Hz, J\(_2=5.3\) Hz, 1H), 2.91 (dd, J\(_1=19.1\) Hz, J\(_2=3.5\) Hz, 1H), 2.87 (m, 1H), 2.17 (s, 3H) ppm; \(^{13}C\) NMR (125 MHz, CDCl\(_3\)): 213.7, 206.2, 200.7, 138.9, 133.4, 129.2 (2C), 128.7 (2C), 59.9, 46.0, 45.6, 41.9, 41.7, 29.7 ppm; \([\alpha]_D^{20}=-14\) (c 1.0, MeOH); HRMS (Orbitrap ESI): calcd for C\(_{15}\)H\(_{16}\)ClO\(_3\): 279.0782 [M+H]^+; found 279.0780.

**(1R,2S,5S)-5-(4-ethylphenyl)-3-oxo-2-(2-oxopropyl)cyclopentane-1-carbaldehyde (3d)**

Yield = 16.9 mg (62%) of a yellow oil.

\(^1H\) NMR (500 MHz, CDCl\(_3\)): 9.65 (d, J=2.1 Hz, 1H), 7.27 (d, J=8.1 Hz, 2H), 7.19 (d, J=8.1 Hz, 2H), 3.43 (td, J\(_1=11.5\) Hz, J\(_2=8.3\) Hz, 1H), 3.26 (td, J\(_1=11.2\) Hz, J\(_2=2.1\) Hz, 1H), 3.04 (dd, J\(_1=19.0\) Hz, J\(_2=5.4\) Hz, 1H), 2.91 (dd, J\(_1=19.0\) Hz, J\(_2=3.6\) Hz, 1H), 2.86 (dd, J\(_1=18.6\) Hz, J\(_2=8.3\) Hz, 1H), 2.76 (dd, J\(_1=18.6\) Hz, J\(_2=11.9\) Hz, 1H), 2.75 (m, 1H), 2.64 (q, J=7.6 Hz, 2H), 2.16 (s, 3H), 1.23 (t, J=7.6 Hz, 2H) ppm; \(^{13}C\) NMR (125 MHz, CDCl\(_3\)): 214.4, 206.1, 201.4, 143.6, 137.4, 128.5 (2C), 127.2 (2C), 60.0, 46.0, 45.8, 42.2, 41.9, 29.7, 28.4, 15.5 ppm; \([\alpha]_D^{20}=+40\) (c 1.0, MeOH); HRMS (Orbitrap ESI): calcd for C\(_{17}\)H\(_{21}\)O\(_3\): 273.1485 [M+H]^+; found 273.1480.

**(1R,2S,5S)-5-(2-methoxyphenyl)-3-oxo-2-(2-oxopropyl)cyclopentane-1-carbaldehyde (3e)**

Yield = 17.3 mg (63%) of a yellow oil.

\(^1H\) NMR (500 MHz, CDCl\(_3\)): 9.60 (d, J=2.8 Hz, 1H), 7.32 (dd, J\(_1=7.5\) Hz, J\(_2=1.5\) Hz, 1H), 7.26 (m, 1H), 6.97 (td, J\(_1=7.5\) Hz, J\(_2=1.0\) Hz, 1H), 6.89 (d, J=8.2 Hz, 1H), 3.83 (m, 1H), 3.82 (s, 3H), 3.20 (td, J\(_1=11.0\) Hz, J\(_2=2.8\) Hz, 1H), 2.92 (m, 2H), 2.87-2.79 (m, 3H), 2.15 (s, 3H) ppm; \(^{13}C\) NMR (125 MHz, CDCl\(_3\)): 214.8, 205.9, 201.2, 157.0, 128.5, 127.9, 127.5, 121.0, 110.7, 59.0, 55.1, 46.0, 43.1, 41.8, 36.1, 29.8 ppm; \([\alpha]_D^{20}=+20\) (c 0.5, MeOH); HRMS (Orbitrap ESI): calcd for C\(_{16}\)H\(_{10}\)O\(_4\): 275.1278 [M+H]^+; found 275.1277.
(1R,2S,5S)-5-(2-fluorophenyl)-3-oxo-2-(2-oxopropyl)cyclopentane-1-carbaldehyde (3f)

Yield = 17.0 mg (65%) of a yellow oil.

\[^1\text{H}\text{ NMR (500 MHz, CDCl}_3\text{): 9.64 (d, }J=1.7 \text{ Hz, 1H), 7.40 (td, }J_1=7.6 \text{ Hz, }J_2=1.5 \text{ Hz, 1H), 7.27 (m, 1H), 7.16 (t, }J=7.5 \text{ Hz, 1H), 7.10 (m, 1H), 3.78 (td, }J_1=11.5 \text{ Hz, }J_2=8.5 \text{ Hz, 1H), 3.27 (td, }J_1=11.3 \text{ Hz, }J_2=2.6 \text{ Hz, 1H), 3.00 (dd, }J_1=19.0 \text{ Hz, }J_2=5.5 \text{ Hz, 1H), 2.94 (dd, }J_1=19.0 \text{ Hz, }J_2=3.6 \text{ Hz, 1H), 2.87 (dd, }J_1=18.6 \text{ Hz, }J_2=8.5 \text{ Hz, 1H), 2.80 (m, 1H), 2.77 (dd, }J_1=18.6 \text{ Hz, }J_2=11.8 \text{ Hz, 1H), 2.16 (s, 3H) ppm; }\[^{13}\text{C NMR (125 MHz, CDCl}_3\text{): 213.7, 206.0, 200.6, 160.8 (d, }J=245.0 \text{ Hz), 129.1 (d, }J=8.7 \text{ Hz), 128.2 (d, }J=12.5 \text{ Hz), 124.8 (d, }J=2.5 \text{ Hz), 115.9 (d, }J=22.5 \text{ Hz), 58.8, 46.0, 43.8, 41.9, 35.1 (d, }J=1.75 \text{ Hz, MeOH); HRMS (Orbitrap ESI): calcd for C\text{\textsubscript{15}}H\text{\textsubscript{16}}FO\text{\textsubscript{3}}: 263.1078 [M+H\textsuperscript{+}]\text{; found 263.1080.}\]

(2S,3R,4S)-3-(hydroxymethyl)-2-(2-oxopropyl)-4-phenylcyclopentan-1-one (7a)

Yield = 9.9 mg (67%) of a yellow oil.

\[^1\text{H NMR (500 MHz, CDCl}_3\text{): 7.35-7.23 (m, 5H), 3.51 (m, 2H), 3.30 (td, }J_1=11.5 \text{ Hz, }J_2=8.3 \text{ Hz, 1H), 3.24 (m, 1H), 2.84 (dd, }J_1=19.0 \text{ Hz, }J_2=8.3 \text{ Hz, 1H), 2.69 (m, 2H), 2.53 (dd, }J_1=19.0 \text{ Hz, }J_2=11.7 \text{ Hz, 1H), 2.50 (t, }J=6.4 \text{ Hz, 1H), 2.23 (s, 3H), 2.04 (m, 1H) ppm; }\[^{13}\text{C NMR (125 MHz, CDCl}_3\text{): 213.7, 206.0, 200.6, 160.8 (d, }J=245.0 \text{ Hz), 129.1 (d, }J=8.7 \text{ Hz), 128.2 (d, }J=12.5 \text{ Hz), 124.8 (d, }J=2.5 \text{ Hz), 115.9 (d, }J=22.5 \text{ Hz), 58.8, 46.0, 43.8, 41.9, 35.1 (d, }J=1.75 \text{ Hz, MeOH); HRMS (Orbitrap ESI): calcd for C\text{\textsubscript{15}}H\text{\textsubscript{19}}O\text{\textsubscript{3}}: 247.1329 [M+H\textsuperscript{+}]\text{; found 247.1326; HPLC (DAICEL Chiralpak AD-H, }n\text{-hexane/2-propanol = 90/10, flow = 0.8 mL/min, detection at 254 nm, retention time = 18.9 min, ee = >99%.}\]

Representative NOEs

(2S,3R,4S)-3-(hydroxymethyl)-4-(4-methoxyphenyl)-2-(2-oxopropyl)cyclopentan-1-one (7b)

Yield = 10.4 mg (63%) of a yellow oil.

\[^1\text{H NMR (500 MHz, CDCl}_3\text{): 7.20 (d, }J=8.6 \text{ Hz, 2H), 6.87 (d, }J=8.6 \text{ Hz, 2H), 3.80 (s, 3H), 3.50 (m, 2H), 3.25 (m, 2H), 2.81 (dd, }J_1=19.0 \text{ Hz, }J_2=8.3 \text{ Hz, 1H), 2.67 (m, 2H), 2.48 (m, 1H), 2.47 (dd, }J_1=19.0 \text{ Hz, }J_2=11.7 \text{ Hz, 1H), 2.23 (s, 3H), 1.98 (tt,
\( J_1 = 11.4 \text{ Hz}, J_2 = 3.4 \text{ Hz, 1H) ppm; } \) 
\( ^{13} \text{C NMR (125 MHz, CDCl}_3): 216.7, 208.5, 158.6, 133.3, 128.6 (2C), 114.1 (2C), 59.9, 55.3, 52.9, 46.8, 45.8, 42.5, 41.0, 29.9 ppm; [\alpha]_D^{20} = +28 \text{ (c 0.5, MeOH); HRMS (Orbitrap ESI): calcd for C}_{16}H_{21}O_4: 277.1434 \text{ [M+H]}^+; found 277.1431; HPLC (DAICEL Chiralpak AD-H, n-hexane/2-propanol = 90/10, flow = 0.8 mL/min, detection at 254 nm, retention time = 25.5 min (major), 32.7 min (minor), ee = 98\%.}

\((2S,3R,4S)-4-(4-chlorophenyl)-3-(hydroxymethyl)-2-(2-oxopropyl)cyclopentan-1-one (7c)\)

\( \text{Yield = 10.9 mg (65%) of a yellow oil.} \)
\( ^1H \text{ NMR (500 MHz, CDCl}_3): 7.31 (d, } J=8.4 \text{ Hz, 2H}, 7.22 (d, J=8.4 Hz, 2H), 3.48 (brs, 2H), 3.30 (td, } J_1=11.5 \text{ Hz, } J_2=8.4 \text{ Hz, 1H), 3.24 (m, 1H), 2.82 (dd, } J_1=19.0 \text{ Hz, } J_2=8.4 \text{ Hz, 1H), 2.69 (m, 2H), 2.48 (m, 1H), 2.47 (dd, } J_1=19.0 \text{ Hz, } J_2=11.8 \text{ Hz, 1H), 2.23 (s, 3H), 1.99 (tt, } J_1=11.3 \text{ Hz, } J_2=3.1 \text{ Hz, 1H) ppm; } \) 
\( ^{13} \text{C NMR (125 MHz, CDCl}_3): 216.0, 208.4, 140.0, 132.7, 129.0 (2C), 128.9 (2C), 59.5, 52.6, 46.7, 45.6, 42.4, 41.1, 29.9 ppm; [\alpha]_D^{20} = +24 \text{ (c 0.5, MeOH); HRMS (Orbitrap ESI): calcd for C}_{15}H_{18}ClO_3: 281.0939 \text{ [M+H]}^+; found 281.0935; HPLC (DAICEL Chiralpak AD-H, n-hexane/2-propanol = 90/10, flow = 0.8 mL/min, detection at 254 nm, retention time = 20.4 min, ee >99\%.} \)

\((2S,3R,4S)-4-(4-ethylphenyl)-3-(hydroxymethyl)-2-(2-oxopropyl)cyclopentan-1-one (7d)\)

\( \text{Yield = 10.0 mg (61%) of a yellow oil.} \)
\( ^1H \text{ NMR (500 MHz, CDCl}_3): 7.20 (d, } J=8.3 \text{ Hz, 2H), 7.17 (d, } J=8.3 \text{ Hz, 2H), 3.51 (m, 2H), 3.26 (m, 2H), 2.82 (dd, } J_1=19.1 \text{ Hz, } J_2=8.2 \text{ Hz, 1H), 2.68 (m, 2H), 2.63 (q, } J=7.6 \text{ Hz, 2H), 2.51 (dd, } J_1=19.1 \text{ Hz, } J_2=11.8 \text{ Hz, 1H), 2.48 (m, 1H), 2.23 (s, 3H), 2.01 (tt, } J_1=11.5 \text{ Hz, } J_2=3.3 \text{ Hz, 1H), 1.23 (t, } J=7.6 \text{ Hz, 3H) ppm; } \) 
\( ^{13} \text{C NMR (125 MHz, CDCl}_3): 216.7, 208.5, 143.0, 138.6, 128.2 (2C), 127.6 (2C), 60.0, 52.8, 46.9, 45.8, 42.5, 41.4, 29.9, 28.4, 15.5 ppm; [\alpha]_D^{20} = +28 \text{ (c 0.5, MeOH); HRMS (Orbitrap ESI): calcd for C}_{17}H_{23}O_3: 275.1642 \text{ [M+H]}^+; found 275.1641; HPLC (DAICEL Chiralpak AD-H, n-hexane/2-propanol = 90/10, flow = 0.8 mL/min, detection at 254 nm, retention time = 15.1 min, ee >99\%.} \)

\((2S,3R,4S)-3-(hydroxymethyl)-4-(2-methoxyphenyl)-2-(2-oxopropyl)cyclopentan-1-one (7e)\)

\( \text{Yield = 10.4 mg (63%) of a yellow oil.} \)
\( ^1H \text{ NMR (500 MHz, CDCl}_3): 7.27-7.22 (m, 2H), 6.96 (t, } J=7.6 \text{ Hz, 1H), 6.90 (d, } J=8.2 \text{ Hz, 1H), 3.84 (s, 3H), 3.62 (td, } J_1=11.0 \text{ Hz, } J_2=9.0 \text{ Hz, 1H), 3.50 (m, 2H), 3.13 (m, 1H), 2.77-2.64 (m, 4H), 2.58 (brt, } J=6.2 \text{ Hz, 1H), 2.21 (s, 3H), 2.20 (m, 1H) ppm; } \) 
\( ^{13} \text{C NMR (125 MHz, CDCl}_3): 217.3, 208.1, 157.5, 129.2, 128.0, 127.9, 121.1, 110.8, \)
60.4, 55.4, 50.7, 46.8, 43.6, 42.2, 35.6, 30.0 ppm; \([\alpha]_D^{20} = +54 (c \ 1.0, \text{MeOH})\); HRMS (Orbitrap ESI): caleedor C_{16}H_{21}O_{4}: 277.1439 \[[M+H]^+\]; found 277.1431; HPLC (DAICEL Chiralpak AD-H, \(n\)-hexane/2-propanol = 90/10, flow = 0.8 mL/min, detection at 254 nm, retention time = 23.8 min, ee = >99%.

(2S,3R,4S)-4-(2-fluorophenyl)-3-(hydroxymethyl)-2-(2-oxopropyl)cyclopentan-1-one (7f) Yield = 9.7 mg (61%) of a yellow oil.

\(^1\)H NMR (500 MHz, CDCl\(_3\)): 7.31 (td, \(J_1=7.5\) Hz, \(J_2=1.7\) Hz, 1H), 7.23 (m, 1H), 7.13 (td, \(J_1=7.5\) Hz, \(J_2=1.1\) Hz, 1H), 7.05 (ddd, \(J_1=10.8\) Hz, \(J_2=8.2\) Hz, \(J_3=1.1\) Hz, 1H), 3.56 (td, \(J_1=11.4\) Hz, \(J_2=8.7\) Hz, 1H), 3.52 (m, 2H), 3.23 (m, 1H), 2.81 (dd, \(J_1=19.0\) Hz, \(J_2=11.7\) Hz, 1H), 2.71 (m, 2H), 2.61 (d, \(J=19.0\) Hz, \(J=11.7\) Hz, 1H), 2.52 (b, \(J=6.4\) Hz, 1H), 2.23 (s, 3H), 2.19 (m, 1H) ppm; \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): 216.2, 208.4, 161.3 (d, \(J=243.7\) Hz), 129.2 (d, \(J=5.0\) Hz), 128.5 (d, \(J=8.7\) Hz), 128.1 (d, \(J=12.5\) Hz), 124.5 (d, \(J=3.7\) Hz), 115.8 (d, \(J=22.5\) Hz), 60.1, 50.9, 46.7, 43.9 (d, \(J=1.2\) Hz), 42.4, 35.5, 29.9 ppm; \([\alpha]_D^{20} = +40 (c \ 1.0, \text{MeOH})\); HRMS (Orbitrap ESI): caleedor C_{15}H_{18}FO_{3}: 265.1234 \[[M+H]^+\]; found 265.1236; HPLC (DAICEL Chiralpak AD-H, \(n\)-hexane/2-propanol = 90/10, flow = 0.8 mL/min, detection at 254 nm, retention time = 18.1 min, ee = >99%.

General procedure for the synthesis of products of type 4 from the corresponding compounds of type 3

 Each compound of type 3 (0.1 mmol, 24.4 mg for 3a, 27.8 mg for 3c, 27.4 mg for 3e) was dissolved in DCE (1 mL) and p-toluenesulfonic acid (PTSA-H\(_2\)O, 13.3 mg, 0.07 mmol) was added. The mixture was heated to 70 °C and stirred for 8 h. After tlc analysis indicated completion of the reaction, the solvent was removed under reduced pressure and the products of type 4 were purified by flash column chromatography (silica gel, petroleum ether:EtOAc). Isolated yields: for 4a = 18.1 mg (80%), for 4c = 20.8 mg (80%) and for 4e = 21.5 mg (84%). All the dr values were measured using \(^1\)H-NMR data for the crude reaction mixture. Racemic mixtures of all the compounds of type 4 were prepared from the corresponding racemic mixtures of compounds of type 3 according to the general experimental procedure described above.
General procedure for the one pot synthesis of carbocycles of type 4 from furan 1a

![Chemical structure of 1a](image)

1. O2, MB, hv; Et3N, Me2S, MeOH
2. OTMS
3. PTSA (0.7 equiv.), DCE, 70 °C, 8 h

2,5-Dimethyl furan 1a (10.7 µL, 0.1 mmol) was dissolved in methanol (2 mL, 50 mM) containing catalytic amounts of methylene blue as photosensitizer (0.1 mM). The solution was cooled using an ice bath. Oxygen was gently bubbled through the solution while it was irradiated by a xenon Variac Eimac Cermax 300 W lamp (VIS 385-740 nm) for 2 min. The solution was then warmed to room temperature and a small amount of Et3N (0.0035 mmol, 3.5% mol, 0.5 µL) was added, followed by Me2S (29 µL, 0.4 mmol). After tlc analysis indicated completion of the reduction (45 min), the solvent was replaced with EtOH/H2O (9/1 v/v, 1 mL). Then, the organocatalyst (6.5 mg, 0.02 mmol, 20 mol%) and the corresponding enal (0.15 mmol, 18.8 µL of 2a, or 25 mg of 2c, or 24.3 mg of 2e) were added and the solution stirred for 24 h at room temperature. After completion of the reaction (as indicated by 1H-NMR of the crude reaction mixture), the solvent was concentrated in vacuo and the products of type 3 were dissolved in DCE (1 mL). Then p-toluenesulfonic acid (PTSA·H2O, 13.3 mg, 0.07 mmol) was added and the mixture was warmed to 70 °C and stirred for 8 h. After completion of the final step (as indicated by tlc analysis), the solvent was removed under reduced pressure and the products of type 4 were purified by flash column chromatography (silica gel, petroleum ether:EtOAc). All the dr values were measured using the 1H-NMR data for the crude reaction mixture and the ee values were measured by chiral HPLC.

When the final aldol/dehydration step is included in our one pot sequences, without isolation and purification of the intermediates, we observed that isolated yields of the final products were a bit better when methylene blue was used instead of rose Bengal. For this reason, we decided to use methylene blue in these one pot protocols. When the same protocol was scaled up to 1 mmol of furan 1a with enal 2c (1.5 mmol) the results were identical.

(3S,3aR,7aR)-3-phenyl-3,3a,7,7a-tetrahydro-1H-indene-1,6(2H)-dione (4a)

The product was prepared according to the general experimental procedure described above. The crude product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 6:1) to furnish 4a as a white solid (13.1 mg, 58%).
\[^1\text{H}\] NMR (500 MHz, CDCl\textsubscript{3}): 7.38 (t, \(J=7.4\) Hz, 2H), 7.30 (tt, \(J_1=7.4\) Hz, 1H), 7.27 (m, 2H), 6.85 (dd, \(J_1=10.2\) Hz, \(J_2=3.3\) Hz, 1H), 6.07 (dd, \(J_1=10.2\) Hz, \(J_2=2.0\) Hz, 1H), 3.58 (m, 1H), 3.23 (m, 1H), 3.02 (q, \(J=7.2\) Hz, 1H), 2.77 (dd, \(J_1=10.2\) Hz, \(J_2=2.0\) Hz, 1H), 2.73 (m, 2H), 2.54 (dd, \(J_1=17.2\) Hz, \(J_2=7.1\) Hz, 1H) ppm; \[^{13}\text{C}\] NMR (125 MHz, CDCl\textsubscript{3}): 215.5, 195.6, 149.1, 141.3, 130.5, 129.0 (2C), 127.4, 126.8 (2C), 45.0, 44.9, 44.5, 43.6, 34.1 ppm; \([\alpha]_D^{25}+30\) (c 1.0, MeOH); HRMS (Orbitrap ESI): calcd for C\textsubscript{15}H\textsubscript{15}O\textsubscript{2}: 227.1067 [M+H]\(^+\); found 227.1068; HPLC (DAICEL Chiralpak AS-H, n-hexane/2-propanol = 50/50, flow = 0.5 mL/min, detection at 254 nm, retention time = 41.5 min, ee = >99%.

Representative NOEs

(3S,3a\textit{R},7a\textit{R})-3-(4-chlorophenyl)-3,3a,7,7a-tetrahydro-1H-indene-1,6(2H)-dione (4c)

The product was prepared according to the general experimental procedure described above. The crude product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 6:1) to furnish 4c as a white solid (13.8 mg, 53%).

\[^1\text{H}\] NMR (500 MHz, CDCl\textsubscript{3}): 7.35 (m, 2H), 7.21 (d, \(J=8.5\) Hz, 2H), 6.82 (dd, \(J_1=10.3\) Hz, \(J_2=3.6\) Hz, 1H), 6.08 (dd, \(J_1=10.3\) Hz, \(J_2=2.0\) Hz, 1H), 3.56 (m, 1H), 3.19 (m, 1H), 3.00 (q, \(J=7.3\) Hz, 1H), 2.75 (m, 2H), 2.66 (dd, \(J_1=19.0\) Hz, \(J_2=6.4\) Hz, 1H), 2.55 (dd, \(J_1=17.2\) Hz, \(J_2=7.1\) Hz, 1H) ppm; \[^{13}\text{C}\] NMR (125 MHz, CDCl\textsubscript{3}): 214.9, 195.3, 148.5, 139.7, 133.3, 130.7, 129.2 (2C), 128.2 (2C), 45.0, 44.4 (2C), 43.6, 34.1 ppm; \([\alpha]_D^{25}+18\) (c 1.0, MeOH); HRMS (Orbitrap ESI): calcd for C\textsubscript{15}H\textsubscript{14}ClO\textsubscript{2}: 261.0677 [M+H]\(^+\); found 261.0671; HPLC (DAICEL Chiralpak OD, n-hexane/2-propanol = 50/50, flow = 0.5 mL/min, detection at 254 nm, retention time = 28.4 min (major), 34.2 min (minor), ee = >99%.

(3S,3a\textit{R},7a\textit{R})-3-(2-methoxyphenyl)-3,3a,7,7a-tetrahydro-1H-indene-1,6(2H)-dione (4e)

The product was prepared according to the general experimental procedure described above. The crude product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 4:1) to furnish 4e as a white solid (14.1 mg, 55%).

\[^1\text{H}\] NMR (500 MHz, CDCl\textsubscript{3}): 7.29 (td, \(J=7.8\) Hz, \(J=1.4\) Hz, 1H), 6.94 (m, 3H), 6.06 (dd, \(J_1=10.2\) Hz, \(J_2=2.2\) Hz, 1H), 3.89 (s, 3H), 3.87 (m, 1H), 3.30 (m, 1H), 2.92 (q, \(J=6.6\) Hz, 1H), 2.85 (dd, \(J_1=17.2\) Hz, \(J_2=5.4\) Hz, 1H), 2.72 (dd, \(J_1=19.2\) Hz, \(J_2=4.7\) Hz, 1H), 2.63 (dd, \(J_1=19.2\) Hz, \(J_2=8.6\) Hz, 1H) ppm; \[^{13}\text{C}\] NMR (125 MHz,
CDCl$_3$): 216.7, 195.9, 157.0, 150.5, 139.8, 128.4, 126.5, 120.6, 110.7, 55.4, 44.6, 42.5, 41.5, 38.8, 34.3 ppm; $[\alpha]_D^{25}$=−66 (c 1.0, MeOH); HRMS (Orbitrap ESI): calcd for C$_{16}$H$_{17}$O$_3$: 257.1172 [M+H]$^+$; found 257.1174; HPLC (DAICEL Chiralpak AS-H, n-hexane/2-propanol = 60/40, flow = 0.5 mL/min, detection at 254 nm, retention time = 48.9 min (major), 66.6 min (minor), ee = >99%.

Synthetic procedure that contributed to the assignment of the absolute configuration of the products of type 4, and, consequently, also that of compounds of type 3 and 6

**Synthesis of the carbocycle 9c**

To a solution of diketone 4c (31.2 mg, 0.12 mmol) in dry DCM (2 mL) at -78 °C, Dibal (264 µL, 1.0 M in Hexanes, 0.264 mmol) was added dropwise. The solution was stirred for 1 h at the same temperature. After the complete consumption of the starting material, as indicated by tlc analysis, the reaction was quenched with saturated aqueous Rochelle’s salt (1 mL) and DCM (5 mL) was added. The biphasic suspension was stirred for 30 min at rt. The aqueous phase was separated and extracted with DCM (5× 2mL). The combined organic phases were dried over Na$_2$SO$_4$ and concentrated under reduced pressure to afford a 4.3/1.3/1.0 mixture of 4 diastereoisomers of diol 8c (determined by $^1$H-NMR). Diol 8c was used in the next step without further purification. A solution of the diol 8c prepared above in dry DCM (2 mL) was added to a flame-dried flask containing activated MnO$_2$ (52.2 mg, 0.6 mmol). The suspension was stirred vigorously at rt for 4 h. After completion of the oxidation, (indicated by tlc analysis), the mixture was filtered through a pad of silica gel and the filtrate concentrated in vacuo to afford 9c as a 2.4/1 mixture of diastereoisomers (separable). The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 2:1) to furnish the major diastereoisomer of 9c as a yellow oil (12.6 mg, 40% over two steps).

$^1$H NMR (500 MHz, CDCl$_3$): 7.32 (d, $J$=8.4 Hz, 2H), 7.20 (d, $J$=8.4 Hz, 2H), 6.76 (dd, $J_1$=10.1 Hz, $J_2$=3.8 Hz, 1H), 6.00 (dd, $J_1$=10.1 Hz, $J_2$=1.1 Hz, 1H), 4.52 (m, 2H), 3.29 (dd, $J_1$=10.4 Hz, $J_2$=7.7 Hz, 1H), 2.85 (m, 2H), 2.64 (m, 2H), 2.20 (ddd, $J_1$=13.7 Hz, $J_2$=8.1 Hz, $J_3$=2.5 Hz, 1H), 2.00 (ddd, $J_1$=13.7 Hz, $J_2$=10.4 Hz, $J_3$=5.0 Hz, 1H), 1.77 (d, $J$=4.0 Hz, 1H) ppm; $^{13}$C NMR (125 MHz, CDCl$_3$): 198.7, 150.2, 142.4, 132.4, 128.9 (2C), 128.5 (2C), 127.9, 76.1, 49.0, 45.7, 42.6, 42.4, 36.2 ppm; $[\alpha]_D^{20}$=+160 (c 0.5, MeOH); HRMS (Orbitrap ESI): calcd for C$_{15}$H$_{16}$ClO$_2$: 263.0833 [M+H]$^+$; found 263.0834.
Mosher ester analysis applied to compound 9c

The absolute configuration of compound 9c was determined using chiral MTPA derivatives. The esterification of compound 9c with R- and S-MTPA was performed as follows:

To a solution of 9c (6.3 mg, 0.024 mmol) in dry CH₂Cl₂ at rt, DCC (10 mg, 0.048 mmol), the corresponding R- or S-MTPA (11.2 mg, 0.048 mmol) and a catalytic amount of 4-DMAP (0.3 mg, 10 mol%) were added and the solution was stirred for 24 h. After completion of the reaction, as indicated by tlc analysis, the mixture was filtered and the organic solvent was removed from the filtrate under reduced pressure. The residue was purified by flash column chromatography (silica gel, Hexane : EtOAc 3:1) to afford the corresponding R- or S-MTPA ester of 9c as a slightly yellow oil in both cases. Yield for R-MTPA = 4.8 mg (42%) and for S-MTPA = 5.2 mg (45%).

\[ \text{Representative NOEs of R- and S-MTPA ester of compound 9c} \]

\[ \text{1H NMR (500 MHz, CDCl}_3\text{): 7.50 (m, 2H), 7.43 (m, 3H), 7.33 (d, } J=8.4 \text{ Hz, 2H), 7.17 (d, } J=8.4 \text{ Hz, 2H), 6.64 (dd, } J_r=10.2 \text{ Hz, } J_s=4.5 \text{ Hz, 1H), 5.97 (dd, } J_r=10.2 \text{ Hz, } J_s=1.5 \text{ Hz, 1H), 5.61 (td, } J_r=6.4 \text{ Hz, } J_s=4.2 \text{ Hz, 1H), 3.51 (s, 3H), 3.19 (q, } J=9.3 \text{ Hz, 1H), 3.13 (m, 1H), 2.82 (m, 1H), 2.47-2.30 (m, 4H) ppm.} \]

\[ \text{1H NMR (500 MHz, CDCl}_3\text{): 7.49 (m, 2H), 7.43 (m, 3H), 7.31 (d, } J=8.4 \text{ Hz, 2H), 7.07 (d, } J=8.4 \text{ Hz, 2H), 6.45 (dd, } J_r=10.2 \text{ Hz, } J_s=3.9 \text{ Hz, 1H), 5.86 (dd, } J_r=10.2 \text{ Hz, } J_s=1.9 \text{ Hz, 1H), 5.48 (td, } J_r=5.4 \text{ Hz, } J_s=2.9 \text{ Hz, 1H), 3.53 (d, } J=1.1 \text{ Hz, 3H), 3.06 (m, 1H), 2.79 (tdd, } J_r=8.5 \text{ Hz, } J_s=3.9 \text{ Hz, } J_s=1.9 \text{ Hz, 1H), 2.73 (m, 1H), 2.54 (dd, } J_r=17.3 \text{ Hz, } J_s=7.4 \text{ Hz, 1H), 2.50 (dd, } J_r=17.3 \text{ Hz, } J_s=6.4 \text{ Hz, 1H), 2.27 (ddd, } J_r=14.6 \text{ Hz, } J_s=8.1 \text{ Hz, } J_s=2.9 \text{ Hz, 1H), 2.14 (ddd, } J_r=15.6 \text{ Hz, } J_s=10.2 \text{ Hz, } J_s=5.4 \text{ Hz, 1H) ppm.} \]

Representative NOEs of R- and S-MTPA ester of compound 9c

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\(^5\) J. M. Seco, E. Quiñoa, R. Riguera, Chem. Rev., 2004, 104, 17-117.
The absolute configuration was assigned after comparing the $^1$H NMR spectra of the $R$- and $S$-MTPA esters of 9c. The corresponding differences in the chemicals shifts ($\Delta \delta_{RS}$ ppm) are reported below:

\begin{align*}
\text{OMTPA} & \quad \text{O} \\
\quad & \quad \text{Cl} \\
\quad & \quad \text{H} \\
\quad & \quad \text{H} \\
\quad & \quad \text{H} \\
\quad & \quad \text{H} \\
\quad & \quad 0.0972 \\
\quad & \quad 0.1477 \\
\end{align*}

Synthesis of cyclopentanone 5a from furan 1b

Disubstituted furan 1b (16.6 mg, 0.1 mmol) was dissolved in methanol (2 mL, 50 mM) containing catalytic amounts of rose Bengal as photosensitizer (0.1 mM). The solution was cooled using an ice bath. Oxygen was gently bubbled through the solution while it was irradiated by a xenon Variac Eimac Cermax 300 W lamp (VIS 385-740 nm) for 2 min. Then the solution was warmed to room temperature and Me$_2$S (29 µL, 0.4 mmol) was added. After tlc analysis indicated completion of the reduction (45 min), the solvent was replaced with EtOH/H$_2$O (9/1 v/v, 1 mL). Then, the organocatalyst (6.5 mg, 0.02 mmol, 20 mol%) and enal 2a (12.6 µL, 0.1 mmol) were added and the solution was warmed to 50 °C and stirred for 24 h. After completion of the reaction (as indicated by $^1$H-NMR of the crude reaction mixture), the solution was concentrated in vacuo to afford a 9/1 mixture of products 5a (dr 1.2/1) and 5a' (determined by the $^1$H-NMR of the crude reaction mixture). The product 5a was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 10:1 → 5:1). The dr value of 5a had increased to 1.7/1 after the chromatographic purification. Yield = 22 mg (70%) of a yellow oil.

$^1$H NMR (500 MHz, CDCl$_3$): δ 9.71 (d, $J$=2.5 Hz, 1H for major), 9.60 (d, $J$=1.9 Hz, 1H for minor), 7.38-7.25 (m, 3H for major plus 5H for minor), 7.18 (d, $J$=7.5 Hz, 2H for major), 3.75 (t, $J$=9.2 Hz, 1H for major), 3.32 (td, $J_1$=9.8 Hz, $J_2$=2.5 Hz, 1H for major), 3.22 (td, $J_1$=11.2 Hz, $J_2$=1.9 Hz, 1H for minor), 3.06 (m, 1H for major plus 2H for minor), 2.95 (m, 1H for major plus 1H for minor), 2.78 (m, 1H for major plus 1H for minor), 2.67 (ddd, $J_1$=10.9 Hz, $J_2$=5.0 Hz, $J_3$=3.7 Hz, 1H for minor), 2.61 (q, $J$=7.7 Hz, 1H for major), 2.18 (s, 3H for major), 2.16 (s, 3H for minor), 1.64-1.43 (m, 2H for major plus 2H for minor), 1.19-1.02 (m, 6H for major plus 6H for minor), 0.77 (t, $J$=6.8 Hz, 3H for minor), 0.75 (t, $J$=7.0 Hz, 3H for
major) ppm; $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 216.2 (1C for major plus 1C for minor), 206.3 (minor), 205.9 (major), 201.5 (minor), 201.1 (major), 140.2 (minor), 137.7 (major), 129.0 (2C for minor), 128.7 (2C for major), 128.3 (2C for major), 127.6 (3C for minor), 127.3 (major), 58.8 (minor), 55.9 (major), 55.5 (minor), 51.4 (major), 48.9 (minor), 45.4 (minor), 45.3 (major), 44.8 (major), 42.5 (major), 41.9 (minor), 31.7 (minor), 31.5 (major), 29.9 (major), 29.8 (minor), 28.3 (minor), 26.9 (major), 26.8 (major), 26.0 (minor), 22.3 (minor), 22.2 (major), 13.9 (1C for major plus 1C for minor) ppm.

In order to investigate the source of the regioselectivity, we isolated the minor isomer 5a’. This isomer was dissolved in EtOH/H$_2$O (9/1, 0.1 M) and the organocatalyst (20 mol%) added. The resulting solution was heated to 50 °C and stirred for 24 h. No formation of isomer 5a was seen. This result suggests that it is not a reversible process that is responsible for the 9:1 final ratio of the organocatalytic reaction.

(1R,2S,5S)-3-oxo-2-(2-oxooctyl)-5-phenylcyclopentane-1-carbaldehyde (5a’)

$^1$H NMR (500 MHz, CDCl$_3$): 9.65 (d, $J$=2.2 Hz, 1H), 7.39-7.28 (m, 5H), 3.46 (td, $J_1$=11.6 Hz, $J_2$=8.3 Hz, 1H), 3.30 (td, $J_1$=11.2 Hz, $J_2$=2.2 Hz, 1H), 3.03 (dd, $J_1$=18.9 Hz, $J_2$=5.3 Hz, 1H), 2.91-2.74 (m, 4H), 2.41 (m, 2H), 1.56 (m, 2H), 1.33-1.24 (m, 6H), 0.88 (t, $J$=6.9 Hz, 3H) ppm; $^{13}$C NMR (125 MHz, CDCl$_3$): 214.3, 208.8, 201.2, 140.3, 129.1 (2C), 127.6, 127.3 (2C), 60.0, 46.1, 45.7, 42.6 (2C), 40.9, 31.5, 28.7, 23.7, 22.4, 14.0 ppm.

We propose that thermodynamic control explains the regioselectivity seen in the reaction of unsymmetrical enediones, with products of the more stable enolate (or enamine) of the enedione (such as, 1biii) being favoured. The more thermodynamically stable enolate (or enamine) has a longer lifetime in which to react with the LUMO-lowered enals. Since the reaction conditions favor the thermodynamic outcome, the enediones predominantly react from the more highly substituted methylene position.
Synthesis of cyclopentanone 5b from furan 1d

Disubstituted furan 1d (12.4 mg, 0.1 mmol) was dissolved in methanol (2 mL, 50 mM) containing catalytic amounts of rose Bengal as photosensitizer (0.1 mM). The solution was cooled using an ice bath. Oxygen was gently bubbled through the solution while it was irradiated by a xenon Variac Eimac Cermax 300 W lamp (VIS 385-740 nm) for 2 min. Then the solution was warmed to room temperature and Me2S (29 µL, 0.4 mmol) was added. After TLC analysis indicated completion of the reduction (45 min), the solvent was replaced with EtOH/H2O (9/1 v/v, 1 mL). The organocatalyst (6.5 mg, 0.02 mmol, 20 mol%) and enal 2a (12.6 µL, 0.1 mmol) were added and the solution was warmed to 50 °C and stirred for 24 h. After completion of the reaction (as indicated by 1H-NMR of the crude reaction mixture), the solution was concentrated in vacuo to afford 5b with dr 1.1/1 as determined by the 1H-NMR of the crude reaction mixture. The product 5b was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 10:1 → 5:1). The dr value for 5b had changed to 1/2 after the chromatographic purification. Yield = 17.4 mg (64%) of a yellow oil.

1H NMR (500 MHz, CDCl3): δ 9.68 (d, J=2.9 Hz, 1H for minor), 9.60 (d, J=2.2 Hz, 1H for major), 7.38-7.27 (m, 5H for major plus 3H for minor), 7.21 (d, J=7.2 Hz, 2H for minor), 3.73 (dd, J1=11.2 Hz, J2=8.8 Hz, 1H for minor), 3.45 (td, J1=10.8 Hz, J2=2.8 Hz, 1H for major), 3.30 (td, J1=11.1 Hz, J2=2.2 Hz, 1H for major), 3.07 (dd, J1=18.8 Hz, J2=5.4 Hz, 1H for major), 2.96 (m, 2H for minor), 2.91-2.76 (m, 3H for major plus 2H for minor), 2.69 (ddd, J1=11.0 Hz, J2=5.4 Hz, J3=3.5 Hz, 1H for major), 2.43 (m, 2H for major plus 2H for minor), 1.07 (d, J=6.8 Hz, 3H for major), 1.05 (t, J=7.3 Hz, 3H for minor), 1.04 (t, J=7.3 Hz, 3H for major), 0.84 (d, J=7.7 Hz, 3H for minor) ppm; 13C NMR (125 MHz, CDCl3): δ 216.8 (minor), 216.3 (major), 209.1 (major), 208.7 (minor), 201.4 (major), 201.3 (minor), 139.3 (major), 137.2 (minor), 129.0 (2C for major), 128.7 (2C for minor), 128.3 (2C for minor), 127.6 (3C for major), 127.3 (minor), 58.3 (major), 54.8 (minor), 51.3 (major), 51.2 (major), 46.2 (minor), 45.7 (minor), 45.6 (minor), 44.9 (major), 40.7 (major), 40.2 (minor), 35.9 (minor), 35.6 (major), 12.6 (minor), 12.4 (major), 7.6 (minor), 7.5 (major) ppm.

Representative NOEs of the isolated mixture of diastereoisomers
Each disubstituted furan of type 1 (0.1 mmol, 16.6 mg for 1b, 15 mg for 1c, 12.4 mg for 1d) was dissolved in methanol (2 mL, 50 mM) containing catalytic amounts of methylene blue as photosensitizer (0.1 mM). The solution was cooled using an ice bath. Oxygen was gently bubbled through the solution while it was irradiated by a xenon Variac Eimac Cermax 300 W lamp (VIS 385-740 nm) for 2 min. Then the solution was warmed to room temperature and a small amount of Et₃N (0.0035 mmol, 3.5% mol, 0.5 μL) followed by Me₂S (29 μL, 0.4 mmol) were added. After tlc analysis indicated completion of the reduction (45 min), the solvent was replaced with EtOH/H₂O (9/1 v/v, 1 mL). The organocatalyst (6.5 mg, 0.02 mmol, 20% mol) and the corresponding enal (0.1 mmol, 12.6 μL of 2a, or 16.2 mg of 2b, or 16.7 mg of 2c) were added and the solution was warmed to 50 °C and stirred for 24 h. After completion of the reaction (as indicated by ¹H-NMR of the crude reaction mixture), the solvent was concentrated in vacuo and DCE (1 mL) was added. p-Toluenesulfonic acid (PTSA∙H₂O, 13.3 mg, 0.07 mmol) was added, the mixture was then warmed to 70 °C and stirred for 8 h. After completion of the final step (as indicated by tlc analysis), the solvent was removed under reduced pressure and the products of type 6 were purified by flash column chromatography (silica gel, petroleum ether:EtOAc). All the dr values were measured using the ¹H-NMR data for the crude reaction mixture. When the same protocol was scaled up to 1 mmol of furan 1b and enal 2a (1 mmol), the results were identical. Racemic mixtures of all the compounds were prepared according to the general experimental procedure described above using a mixture of 10 mol% of (S)-(−)-α,α-diphenyl-2-pyrrolidinemethanol trimethylsilyl ether (3.2 mg, 0.01 mmol) and 10 mol% of (R)-(−)-α,α-diphenyl-2-pyrrolidinemethanol trimethylsilyl ether (3.2 mg, 0.01 mmol) as the organocatalyst.
(2S,3R,3aR,7aR)-2-pentyl-3-phenyl-3,3a,7,7a-tetrahydro-1H-indene-1,6(2H)-dione (6a)

The product was prepared according to the general experimental procedure described above to furnish products with a dr 13/1 (separable). The crude residue was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 10:1 → 5:1) to furnish 6a as a yellow oil (18.6 mg, 63%).

\(^1\)H NMR (500 MHz, CDCl\(_3\)): δ 7.40 (t, J=7.4 Hz, 2H), 7.33-7.28 (m, 3H), 6.67 (dd, J\(_1\)=10.2 Hz, J\(_2\)=4.5 Hz, 1H), 6.01 (d, J=10.2 Hz, 1H), 3.22-3.04 (m, 3H), 2.69 (m, 1H), 2.63 (dd, J\(_1\)=16.8 Hz, J\(_2\)=7.1 Hz, 1H), 2.46 (dd, J\(_1\)=16.8 Hz, J\(_2\)=12.6 Hz, 1H), 1.62 (m, 1H), 1.51 (m, 1H), 1.31-1.23 (m, 2H), 1.21-1.10 (m, 4H), 0.78 (t, J=6.9 Hz, 3H), ppm; \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): δ 216.1, 195.8, 148.0, 140.1, 129.2, 129.0 (2C), 127.6, 127.2 (2C), 57.5, 51.8, 45.8, 42.6, 33.8, 31.7, 28.2, 26.3, 22.3, 13.9 ppm; HRMS (OrbitrapESI): calcd for C\(_{20}\)H\(_{25}\)O\(_2\): 297.1849 [M+H]\(^+\); found: 297.1848; [\(\alpha\)]\(_D\)\(^{25}\) +132 (c 1.0, MeOH); HPLC (DAICEL Chiralpak AS-H, n-hexane/2-propanol = 70/30, flow = 0.5 mL/min, detection at 254 nm, retention time = 26.3 min (major), 35.2 min (minor) ee = 99%.

(2S,3R,3aR,7aR)-2-(but-3-en-1-yl)-3-phenyl-3,3a,7,7a-tetrahydro-1H-indene-1,6(2H)-dione (6b)

The product was prepared according to the general experimental procedure described above to furnish products with a dr 13/1 (separable). The crude residue was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 10:1 → 3:1) to furnish 6a as a yellow oil (18.2 mg, 65%).

\(^1\)H NMR (500 MHz, CDCl\(_3\)): δ 7.40 (t, J=7.4 Hz, 2H), 7.34-7.29 (m, 3H), 6.66 (dd, J\(_1\)=10.3 Hz, J\(_2\)=4.4 Hz, 1H), 6.02 (d, J=10.3 Hz, 1H), 5.63 (ddt, J\(_1\)=17.1 Hz, J\(_2\)=10.4 Hz, J\(_3\)=6.5 Hz, 1H), 4.90 (m, 1H), 4.84 (dq, J\(_1\)=17.1 Hz, J\(_2\)=1.6 Hz, 1H), 3.20 (m, 1H), 3.14-3.04 (m, 2H), 2.72 (m, 1H), 2.65 (dd, J\(_1\)=16.9 Hz, J\(_2\)=7.2 Hz, 1H), 2.47 (dd, J\(_1\)=16.9 Hz, J\(_2\)=12.6 Hz, 1H), 1.99 (m, 2H), 1.80 (m, 1H), 1.59 (m, 1H) ppm; \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): δ 215.9, 195.8, 147.8, 139.8, 137.6, 129.3, 129.1 (2C), 127.7, 127.2 (2C), 115.4, 56.5, 52.2, 45.7, 42.7, 34.0, 30.8, 27.7 ppm; HRMS (OrbitrapESI): calcd for C\(_{19}\)H\(_{22}\)O\(_2\): 281.1536 [M+H]\(^+\); found: 281.1535; [\(\alpha\)]\(_D\)\(^{25}\) +108 (c 0.5, MeOH); HPLC (DAICEL Chiralpak AS-H, n-hexane/2-propanol = 60/40, flow = 0.7 mL/min, detection at 254 nm, retention time = 20.9 min (major), 32 min (minor) ee = 99%.

(2S,3R,3aR,7aR)-2,5-dimethyl-3-phenyl-3,3a,7,7a-tetrahydro-1H-indene-1,6(2H)-dione (6c)

The product was prepared according to the general experimental procedure described above to furnish products with a dr 13/1 (separable). The crude residue was purified by flash column...
chromatography (silica gel, petroleum ether:EtOAc = 10:1 → 5:1) to furnish 6c as a yellow oil (12.7 mg, 50%).

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.41 (t, $J=7.4$ Hz, 2H), 7.34-7.29 (m, 3H), 6.42 (m, 1H), 3.22 (m, 1H), 3.11 (m, 1H), 2.93 (t, $J=11.3$ Hz, 1H), 2.68 (dd, $J_1=16.6$ Hz, $J_2=7.3$ Hz, 1H), 2.62 (m, 1H), 2.45 (dd, $J_1=16.6$ Hz, $J_2=13.1$ Hz, 1H), 1.76 (t, $J=1.4$ Hz, 3H), 1.09 (d, $J=6.9$ Hz, 3H) ppm; $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 216.4, 196.2, 142.4, 139.6, 135.6, 129.1 (2C), 127.6, 127.3 (2C), 54.2, 53.3, 45.8, 42.2, 34.4, 16.1, 12.7 ppm; HRMS (OrbitrapESI): calcd for C$_{17}$H$_{19}$O$_2$: 255.1380 [M+H]$^+$; found: 255.1385; $[^a]D$_{26}^0$ = +112 (c 1.0, MeOH), HPLC (DAICEL Chiralpak AS-H, n-hexane/2-propanol = 60/40, flow = 0.5 mL/min, detection at 254 nm, retention time = 19.6 min (major), 21.7 min (minor) ee = 96%.

Representative NOEs

(2S,3R,3aR,7aR)-3-(4-chlorophenyl)-2-pentyl-3,3a,7,7a-tetrahydro-1H-indene-1,6(2H)-dione (6d)

The product was prepared according to the general experimental procedure described above to furnish products with a dr 10:1 (separable). The crude residue was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 10:1 → 3:1) to furnish 6d as a yellow oil (14.8 mg, 45%).

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.38 (d, $J=8.4$ Hz, 2H), 6.64 (dd, $J_1=10.2$ Hz, $J_2=4.7$ Hz, 1H), 6.02 (dd, $J_1=10.2$ Hz, $J_2=0.8$ Hz, 1H), 3.19 (m, 1H), 3.10 (t, $J=10.9$ Hz, 1H), 3.01 (m, 1H), 2.64 (m, 2H), 2.44 (dd, $J_1=16.8$ Hz, $J_2=12.8$ Hz, 1H), 1.61 (m, 1H), 1.51 (m, 1H), 1.24-1.08 (m, 6H), 0.80 (t, $J=7.0$ Hz, 3H) ppm; $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 215.4, 195.5, 147.3, 138.6, 133.4, 129.5, 129.3 (2C), 128.5 (2C), 57.5, 51.3, 45.8, 42.6, 33.8, 31.7, 28.2, 26.4, 22.3, 13.9 ppm; HRMS (OrbitrapESI): calcd for C$_{20}$H$_{24}$ClO$_2$: 331.1459 [M+H]$^+$; found: 331.1457; $[^a]D$_{26}^0$ = +216 (c 0.5, MeOH), HPLC (DAICEL Chiralpak AS-H, n-hexane/2-propanol = 70/30, flow = 0.5 mL/min, detection at 254 nm, retention time = 27.9 min (major), 66.6 min (minor) ee = 99%.

Representative NOEs
(2S,3R,3aR,7aR)-2-(but-3-en-1-yl)-3-(4-methoxyphenyl)-3,3a,7,7a-tetrahydro-1H-indene-1,6(2H)-dione (6e)

The product was prepared according to the general experimental procedure described above to furnish products with a dr 13/1 (separable). The crude residue was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 10:1 → 3:1) to furnish 6e as a yellow oil (13 mg, 42%).

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.21 (d, $J$=8.4 Hz, 2H), 6.93 (d, $J$=8.4 Hz, 2H), 6.67 (dd, $J_1$=10.3 Hz, $J_2$=4.4 Hz, 1H), 6.01 (d, $J$=10.3 Hz, 1H), 5.64 (ddt, $J_1$=17.0 Hz, $J_2$=10.3 Hz, $J_3$=6.6 Hz, 1H), 4.90 (d, $J$=10.3 Hz, 1H), 4.86 (m, 1H), 3.83 (s, 3H), 3.18 (m, 1H), 3.05 (m, 2H), 2.65 (m, 2H), 2.44 (dd, $J_1$=16.8 Hz, $J_2$=12.8 Hz, 1H), 1.99 (m, 2H), 1.78 (m, 1H), 1.57 (m, 1H) ppm; $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 216.0, 195.8, 159.0, 148.0, 137.6, 131.6, 129.2, 128.2 (2C), 115.4, 114.4 (2C), 56.6, 55.3, 51.5, 45.7, 42.9, 34.0, 30.8, 27.6 ppm; HRMS (OrbitrapESI): calcd for C$_{20}$H$_{23}$O$_3$: 311.1642 [M+H]$^+$; found: 311.1642; $[\alpha]_D^{26}$ = +120 (c 0.2, MeOH); HPLC (Chiralcel OD, n-hexane/2-propanol = 70/30, flow = 0.6 mL/min, detection at 254 nm, retention time = 21.8 min (major), 27.7 min (minor) ee = 99%.
Reactor Set-up

- Gas outlet (O₂ or air)
- Ice baths
- Collection vessels
- Pressure regulator
- Gas inlet (O₂ or air)
- LED strip
- Pneumatic nebulizer
- Liquid pump
- 3-way valve
- Filter
- Solvent
- Substrate solution
Figure 1. Schematic representation of NebPhotOX continuous flow reactor set-up. The vertical cylinder has 33 cm length and 6.7 cm diameter.

Figure 2. NebPhotOX in action.

SAFETY CAUTION: Measures were taken to eliminate all possible ignition sources from the fumehood area (sparks or flames; for example, the transformer for the LEDs was kept outside the fumehood) in which the NebPhotOX system was operated. The photoreactor operates 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 the operator wearing safety glasses with side shields and flame resistant safety clothing. The two cooled collection flasks placed in series were prefilled with excess of Me₃S in MeOH (3 equiv in the first flask and 1 equiv in the second flask) for the fast reduction of the hydroperoxides. Even higher excesses of the reducing agent can be used.
General procedure for the synthesis of enantioenriched products of type 3, 4 and 6 from disubstituted furans of type 1 using a continuous flow photoreactor for the photooxygenation step.

2-Substituted furans of type 1 (3 mmol, 324 μL for 1a, 498 mg for 1b) and rose Bengal (0.8 mol%, 24.4 mg) were dissolved in MeOH (total volume 6 mL, 0.5 M). The resulting solutions were transferred to the nebulizer via a liquid pump (flow rate set at 0.7 mL per min) and timing was initiated so that the exact flow rate could be calculated. The solutions were dispersed by the nebulizer into the reaction cylinder which was placed in vertical position using air as nebulizing gas (60 psi backpressure). The cylinder was irradiated by the LED jacket (natural white light 3800–4200 K, 10 W m⁻¹, 1050 Lm m⁻¹). When all the solution had been dispersed (8.6 min, flow rate: 0.70 mL per min, conversion 100%, productivity: 0.35 mmol per min), the timing was stopped and the three-way valve on the uptake line was switched to pure MeOH (3 mL) to flush out the system. The crude solutions were collected in the two cooled spherical flasks placed in series. The two flasks had been pre-charged with Me₂S (9 mmol, 656 μL for the first and 3 mmol, 219 μL for the second) for the rapid reduction of the hydroperoxides formed. The solutions from the two flasks were combined and stirred for a further 45 min, until tlc analysis indicated completion of the reduction. Then the crude solution was concentrated in vacuo for the measurement of the conversions by ¹H NMR.

In the case of the cis-enedione 1ai, the crude reaction mixture was dissolved in EtOH/H₂O (9/1 v/v, 30 mL) and the resulting solution was divided into three equal parts (10 mL each). In each part the corresponding enal (1.5 mmol, 189 μL for 2a, 250 mg for 2c, 243 mg for 2e) followed by the organocatalyst (65 mg, 0.2 mmol) were added. The solution was stirred at room temperature for 24 h. In the synthesis of
cyclopentanones 3a and 3c, the solution was concentrated in vacuo and the products were purified by flash column chromatography (silica gel, petroleum ether : EtOAc). Yield: for 3a = 159 mg (65%) and for 3c = 172 mg (62%). In the synthesis of carbocycle 4e, after the formation of the intermediate 3e, the solvent was replaced by DCE (10 mL) and p-toluenesulfonic acid (PTSA·H₂O, 133 mg, 0.7 mmol) was added. The mixture was warmed to 70 °C and stirred for 8 h. After the final step was complete (as indicated by tlc analysis), the solvent was removed under reduced pressure and the product 4e was purified by flash column chromatography (silica gel, petroleum ether:EtOAc). Yield = 133 mg (52%).

In case of the cis-enedione 1bi, the crude reaction mixture was dissolved in EtOH/H₂O (9/1 v/v, 30 mL) and the resulting solution was divided into three equal parts (15 mL each). In each part the corresponding enal (1.5 mmol, 189 µL for 2a, 250 mg for 2c) followed by the organocatalyst (98 mg, 0.3 mmol) were added. The solution was warmed to 50 °C and stirred for 24 h. After that the solvent was replaced by DCE (15 mL) and p-toluenesulfonic acid (PTSA·H₂O, 200 mg, 0.7 mmol) was added. The mixture was warmed to 70 °C and stirred for 8 h. After the final step was complete (as indicated by tlc analysis), the solvent was removed under reduced pressure and the products of type 6 were purified by flash column chromatography (silica gel, petroleum ether:EtOAc). Yield: for 6a = 244 mg (55%) and for 6d = 242 mg (49%).
Part B: Copies of $^1$H-NMR, $^{13}$C-NMR, COSY, HMBC and NOE spectra

(500 MHz, CDCl$_3$)

(125 MHz, CDCl$_3$)
$^{1}$ai

(500 MHz, CDCl$_3$)

$^{2}$ai

(125 MHz, CDCl$_3$)
1bi
(500 MHz, CDCl₃)

1bi
(125 MHz, CDCl₃)
$\text{Me} \to \text{C} \to \text{O} \to \text{Me}$

(500 MHz, CDCl$_3$)

$\text{Me} \to \text{C} \to \text{O} \to \text{Me}$

(125 MHz, CDCl$_3$)
1bii
(500 MHz, CDCl₃)

1bii
(125 MHz, CDCl₃)
3a

(500 MHz, CDCl₃)

3a

(125 MHz, CDCl₃)
COSY correlations of compound 3a
HSQC correlations of compound 3a
HMBC correlations of compound 3a
Representative NOEs of compound 3a
3b

(500 MHz, CDCl₃)

3b

(125 MHz, CDCl₃)
$\text{Me-O-COOH}$

(500 MHz, CDCl$_3$)

$\text{Me-O-COOH}$

(125 MHz, CDCl$_3$)
3d (500 MHz, CDCl₃)

3d (125 MHz, CDCl₃)
(500 MHz, CDCl$_3$)

7a

(125 MHz, CDCl$_3$)

7a
COSY correlations of compound 7a
Representative NOEs of compound 7a
$7e$

(500 MHz, CDCl$_3$)

$7e$

(125 MHz, CDCl$_3$)
(500 MHz, CDCl₃)

(125 MHz, CDCl₃)
COSY correlations of compound 4a
HSQC correlations of compound 4a
HMBC correlations of compound 4a
Representative NOEs of compound 4a
(500 MHz, CDCl₃)

(125 MHz, CDCl₃)
COSY correlations of the R-MTPA ester of compound 9c
COSY correlations of the S-MTPA ester of compound 9c

Comparison of the $^1$H NMR spectrum of the R and S-MTPA ester of 9c

\[ \Delta \delta_{RS} = -0.0972 \]

\[ \Delta \delta_{RS} = +0.1477 \]
Representative NOEs of the R-MTPA ester of compound 9c
Representative NOEs of the S-MTPA ester of compound 9c
COSY correlations of compound 5b
Representative NOEs of compound 5b
(500 MHz, CDCl₃)

O
O
Ph
C₅H₁₁

6a

(125 MHz, CDCl₃)

O
O
Ph
C₅H₁₁

6a
$^1$H NMR spectra for compounds 6c.

(500 MHz, CDCl$_3$)

(125 MHz, CDCl$_3$)
COSY correlations of compound 6c
HMBC correlations of compound 6c
Representative NOEs of compound 6c
COSY correlations of compound 6d
HMBC correlations of compound 6d
Representative NOEs of compound 6d
S77

(500 MHz, CDCl₃)

6e

(125 MHz, CDCl₃)
Part C: Copies of HPLC chromatograms

Racemic mixture of 7a

(2S,3R,4S)-3-(hydroxymethyl)-2-(2-oxopropyl)-4-phenylcyclopentan-1-one (7a)
Racemic mixture of 7b

(2S,3R,4S)-3-(hydroxymethyl)-4-(4-methoxyphenyl)-2-(2-oxopropyl)cyclopentan-1-one (7b)
Racemic mixture of 7c

(2S,3R,4S)-4-(4-chlorophenyl)-3-(hydroxymethyl)-2-(2-oxopropyl)cyclopentan-1-one (7c)
Racemic mixture of 7d

(2S,3R,4S)-4-(4-ethylphenyl)-3-(hydroxymethyl)-2-(2-oxopropyl)cyclopentan-1-one (7d)
Racemic mixture of $7e$

$(2S,3R,4S)$-3-(hydroxymethyl)-4-(2-methoxyphenyl)-2-(2-oxopropyl)cyclopentan-1-one ($7e$)
Racemic mixture of 7f

(2S,3R,4S)-4-(2-fluorophenyl)-3-(hydroxymethyl)-2-(2-oxopropyl)cyclopentan-1-one (7f)
Racemic mixture of 4a

(3S,3aR,7aR)-3-phenyl-3,3a,7,7a-tetrahydro-1H-indene-1,6(2H)-dione (4a)
Racemic mixture of 4c

(3S,3aR,7aR)-3-(4-chlorophenyl)-3,3a,7,7a-tetrahydro-1H-indene-1,6(2H)-dione (4c)
Racemic mixture of 4e

(3S,3aR,7aR)-3-(2-methoxyphenyl)-3,3a,7a-tetrahydro-1H-indene-1,6(2H)-dione (4e)
Racemic mixture of 6a

(2S,3R,3aR,7aR)-2-pentyl-3-phenyl-3,3a,7,7a-tetrahydro-1H-indene-1,6(2H)-dione (6a)
Racemic mixture of 6b

(2S,3R,3aR,7aR)-2-(but-3-en-1-yl)-3-phenyl-3,3a,7,7a-tetrahydro-1H-indene-1,6(2H)-dione (6b)
Racemic mixture of 6c

(2S,3R,3aR,7aR)-2,5-dimethyl-3-phenyl-3,3a,7,7a-tetrahydro-1H-indene-1,6(2H)-dione (6c)
Racemic mixture of 6d

(2S,3R,3aR,7aR)-3-(4-chlorophenyl)-2-pentyl-3,3a,7,7a-tetrahydro-1H-indene-1,6(2H)-dione (6d)
Racemic mixture of 6e

(2S,3R,3aR,7aR)-2-(but-3-en-1-yl)-3-(4-methoxyphenyl)-3,3a,7,7a-tetrahydro-1H-indene-1,6(2H)-dione (6e)