Tertiary Amine Catalyzed Carbocyclization Sequence to Spirocyclo Hexene Systems Having Vicinal Quaternary Stereocenters

Jindian Duan, Fangyi Cao, Xiaoqin Wang, and Cheng Ma*
Department of Chemistry Zhejiang University 20 Yugu Road, Hangzhou 310027, P.R. China
E-mail: mcorg@zju.edu.cn

Contents

Experimental section S2

General S2

General procedure for the synthesis of cyclic ketone derivatives 1 and 5 S2–S3

Preparation of 2-(2-phenylethylidene)cyclopentanone (9) S4

Procedure for the preparation of 3a S4

General procedure for the preparation of product 4, 6, 8, and 11 S5–S11

References S11

1H NMR and 13C NMR spectra S12–S39
Experimental section

General

All reactions were carried out under nitrogen atmosphere, with dry, freshly distilled solvents in anhydrous conditions. 1,4-Dioxane and THF was distilled from sodium, while dichloromethane and DMF distilled from CaH₂ immediately prior to use. All chemicals were used without further purification as commercially available unless otherwise noted. Thin-layer chromatography (TLC) was performed on silica gel plates (60F-254) using UV-light (254 and 365 nm). Flash chromatography was conducted on silica gel (300–400 mesh). NMR (400 MHz or 500 MHz for ¹H NMR, 100 MHz or 125 MHz for ¹³C NMR) spectra were recorded in CDCl₃ with TMS as the internal standard. High resolution mass spectral (HRMS) analyses were measured using EI techniques. UV detection was monitored at 254 nm. Melting points were obtained in open capillary tubes and were uncorrected.

Cyclic β-oxoaldehydehyaldehydes,¹ β,γ-unsaturated α-keto esters,²,³ substituted 2-alkylidene cyclopentanones ⁹ and ¹⁰ were synthesized according to the literature procedures.

General procedure for the synthesis of cyclic ketone derivatives 1 and 5

2-Alkylidene cyclic ketone derivatives 1 and 5 were prepared by the Wittig reaction of the corresponding cyclic β-oxoaldehyde and triphenylphosphorane as shown as following.

![Scheme](image)

To a solution of cyclic β-oxoaldehyde (2 mmol) in anhydrous CH₂Cl₂ (5 mL), the triphenylphosphorane (2.2 mmol) was added under nitrogen atmosphere and the mixture was stirred at 25 °C for several hours until complete consumption of the aldehyde (as observed by TLC). Then the resulting mixture was concentrated under reduced pressure and purified by column chromatography on silica gel (300–400 mesh) to afford the product 1 or 5.

(E)-Methyl 3-(2-oxocyclopentylidene)propanoate (1a)

Prepared according to general procedure with n-hexane/EtOAc 10:1 as an eluent to afford 1a (302 mg, 90 %) as a colorless oil. The E-configuration of double bond was detected accordingly to the NOESY and COSY spectrums; ¹H NMR (400 MHz, CDCl₃, TMS): δ 6.67–6.63 (m, 1H), 3.72 (s, 3H), 3.20 (d, J = 7.2 Hz, 2H), 2.64–2.60 (m, 2H), 2.38–2.34 (m, 2H), 2.01–1.93 ppm (m, 2H); HRMS (EI): [C₉H₁₂O₃]+, Calc: 168.0786, Found: 168.0788.

Methyl 3-(2-oxocyclohexylidene)propanoate (keto-A)

Prepared according to general procedure with n-hexane /EtOAc 10:1 as an eluent to afford the desired compound as a colorless oil (291 mg, 80 %); this compound existed as a mixture of three unisolatable isomers according to
the $^1$H NMR spectra (keto-A/keto-B/enol-C = 1 : 0.28 : 0.33), the configuration of double bond in keto-A was not detected; HRMS (EI): [C$_{10}$H$_{14}$O$_3$]$^+$, Calc: 182.0943, Found: 182.0944; for keto-A form: $^1$H NMR (400 MHz, CDCl$_3$, TMS): $\delta$ 6.72 (t, $J = 7.2$ Hz, 1H), 3.71 (s, 3H), 3.16 (d, $J = 7.2$ Hz, 2H), 2.51–2.44 (m, 4H), 1.99–1.82 (m, 2H), 1.78–1.70 ppm (m, 2H).

**Methyl 3-(2-oxocycloheptylidene)propanoate**

Prepared according to general procedure with n-hexane /EtOAc 10:1 as an eluent to afford the desired compound (314 mg, 80 %) as a colorless oil; the configuration of double bond was not detected; $^1$H NMR (500 MHz, CDCl$_3$, TMS): $\delta$ 6.67 (t, $J = 7.5$ Hz, 1H), 3.71 (s, 3H), 3.20 (d, $J = 7.0$ Hz, 2H), 2.63–2.60 (m, 2H), 2.44–2.42 (m, 2H), 1.76–1.66 ppm (m, 6H); $^{13}$C NMR (125 MHz, CDCl$_3$, TMS): $\delta$ 204.0, 170.9, 143.2, 129.0, 52.1, 43.2, 33.5, 31.2, 29.3, 27.4, 25.1 ppm; HRMS (EI): [C$_{11}$H$_{16}$O$_3$]$^+$, Calc: 196.1099, Found: 196.1101.

**Ethyl 3-(1-oxo-3,4-dihydronaphthalen-2(1H)-ylidene)propanoate**

Prepared according to general procedure with n-hexane /EtOAc 10:1 as an eluent to afford the desired compound (366 mg, 75 %) as a pale sticky oil; the configuration of double bond was not detected; $^1$H NMR (500 MHz, CDCl$_3$, TMS): $\delta$ 8.10 (d, $J = 7.5$ Hz, 1H), 7.48 (t, $J = 7.5$ Hz, 1H), 7.34 (t, $J = 7.5$ Hz, 1H), 7.27–7.24 (m, 1H), 7.04 (t, $J = 7.5$ Hz, 1H), 4.18 (q, $J = 7.0$ Hz, 2H), 3.30 (d, $J = 7.0$ Hz, 2H), 3.00–2.97 (m, 2H), 2.82–2.80 (m, 2H), 1.28 ppm (t, $J = 7.0$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$, TMS): $\delta$ 186.9, 170.4, 143.6, 137.7, 133.3, 133.2, 130.1, 128.3, 128.2, 127.0, 61.2, 34.0, 28.8, 26.0, 14.2 ppm; HRMS (EI): [C$_{15}$H$_{16}$O$_3$]$^+$, Calc: 244.1099, Found: 244.1103.

**((1S,2R,5R)-5-isopropyl-2-methylcyclohexyl) 3-(2-oxocyclopentylidene)propanoate (5)**

Prepared according to general procedure with n-hexane /EtOAc 20:1 as an eluent to afford 5 (496 mg, 85 %) as a pale sticky oil; the configuration of double bond was not detected; $^1$H NMR (500 MHz, CDCl$_3$, TMS): $\delta$ 6.69–6.66 (m, 1H), 4.74–4.69 (m, 1H), 3.17 (d, $J = 7.5$ Hz, 2H), 2.63–2.60 (m, 2H), 2.36 (t, $J = 7.5$ Hz, 2H), 1.99–1.94 (m, 3H), 1.86–1.80 (m, 1H), 1.69–1.67 (m, 1H), 1.49–1.48 (m, 1H), 1.41–1.36 (m, 1H), 1.09–0.97 (m, 2H), 0.91–0.88 (m, 8H), 0.76–0.74 ppm (m, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$, TMS): $\delta$ 201.2, 164.4, 134.5, 121.5, 69.9, 41.7, 35.6, 33.3, 30.3, 28.9, 26.1, 21.7, 21.1, 18.2, 16.8, 15.5, 14.4, 11.1 ppm; HRMS (EI): [C$_{18}$H$_{28}$O$_3$]$^+$, Calc: 292.2038, Found: 292.2042.
Preparation of 2-(2-phenylethylidene)cyclopentanone (9)

To a solution of phenylacetaldehyde (2.9 g, 24 mmol) in anhydrous CH₂Cl₂ (50 mL), titanium chloride (2.6 mL, 24 mmol) was added at -78˚C for 1h. Then (cyclopent-1-en-1-yloxy)trimethylsilane [5] (3.1 g, 20 mmol) was added over 1h. The reaction mixture was stirred for 8 h at -78˚C, and worked up using saturated NaHCO₃ and ether. Organic layer was washed with brine, dried over anhydrous Na₂SO₄, filtered and evaporated under vacuo. The crude residue obtained was purified by column chromatography (n-hexane/EtOAc 10:1) to yield product 9 (2.2 g, 60%) as a sticky oil.

2-(2-Phenylethylidene)cyclopentanone (9)

The configuration of double bond was not detected; ¹H NMR (400 MHz, CDCl₃, TMS): δ 7.30–7.26 (m, 2H), 7.25–7.17 (m, 3H), 6.70 (t, J = 3 Hz, 1H), 3.48 (d, J = 7.2 Hz, 2H), 2.69–2.66 (m, 2H), 2.00–1.92 ppm (m, 2H); ¹³C NMR (125 MHz, CDCl₃, TMS): δ 207.0, 137.7, 133.7, 129.0, 128.6, 128.4, 38.5, 35.7, 26.7, 19.7 ppm; HRMS (EI): [C₁₃H₁₄O⁺], Calc: 186.1045, Found: 186.1049.

Procedure for the preparation of 3a

To a solution of α-keto ester 2a (57.0 mg, 0.30 mmol) in anhydrous 1,4-dioxane (3 mL), 2-alkylidene cyclopentanone 1a (55.4 mg, 0.33 mmol) and Na₂CO₃ (6.4 mg, 0.06 mmol) were added successively under nitrogen atmosphere. The reaction was stirred at 25 ˚C for 12 h, quenched with H₂O (10 mL) and extracted with CH₂Cl₂ (10 mL × 3). The combined organic layers were dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The resulting oil was purified by column chromatography (n-hexane/EtOAc 10:1) to afford compound 3a (91.3 mg, 85%) as a white solid.

Dimethyl 5-oxo-2-(2-oxocyclopentylidene)methyl)-3-phenylhexanedioate (anti-3a)

White solid, m.p. 145–148 ˚C (ether/n-hexane); ¹H NMR (400 MHz, CDCl₃, TMS): δ 7.29–7.19 (m, 5H), 6.53 (d, J = 10.8 Hz, 1H), 3.85–3.81 (m, 1H), 3.79 (s, 3H), 3.55–3.52 (m, 1H), 3.50 (s, 3H), 3.34–3.18 (m, 2H), 2.63–2.56 (m, 1H), 2.37–2.29 (m, 3H), 1.94–1.88 ppm (m, 2H); ¹³C NMR (100 MHz, CDCl₃, TMS): δ 206.1, 191.4, 170.9, 160.7, 141.5, 133.9, 128.7, 128.5, 127.8, 127.7, 127.4, 53.0, 52.3, 52.0, 42.7, 41.7, 38.4, 29.6, 26.8, 19.5 ppm; IR (KBr): ν 3029, 2952, 1742, 1735, 1715, 1647, 1454, 1437, 1266, 1246, 1213, 1178, 1085; HRMS (EI): [C₂₀H₂₂O₆⁺], Calc: 358.1416, Found: 358.1418.
General procedure for the preparation of 4, 6, 8, and 11

To a solution of α-keto ester 2 (0.30 mmol) in anhydrous 1,4-dioxane (3 mL), 2-alkylidene cyclopentanone 1 (0.33 mmol) and DABCO·6H2O (0.06 mmol, 20 mol %) were added successively under nitrogen atmosphere. The reaction was stirred at 25 °C or 40 °C until completely consumption of the intermediate. The resulting mixture was concentrated under reduced pressure and purified by column chromatography to afford the products.

Dimethyl 6-hydroxy-1-oxo-8-phenylspiro[4.5]dec-9-ene-6,9-dicarboxylate (4a)

\[
\begin{align*}
&\text{O} \\
&\text{CO}_2\text{Me} \\
&\text{Ph} \\
&\text{HO} \\
&\text{CO}_2\text{Me}
\end{align*}
\]

Prepared according to general procedure with n-hexane/acetone 10:1 as an eluent to afford 4a (103 mg, 96 %) as a pale sticky oil; \(^1\text{H NMR}\) (500 MHz, CDCl\(_3\), TMS): \(\delta 7.28–7.25\) (m, 2H), 7.19–7.16 (m, 1H), 7.12–7.11 (m, 2H), 6.71 (d, \(J = 2\) Hz, 1H), 5.18 (d, \(J = 2.5\) Hz, 1H), 4.10–4.06 (m, 1H), 3.67 (s, 3H), 3.49 (s, 3H), 2.63–2.55 (m, 3H), 2.24–2.20 (m, 1H), 2.15–2.03 (m, 2H), 1.97–1.96 (m, 1H), 1.84–1.79 ppm (m, 1H); \(^1\text{C NMR}\) (125 MHz, CDCl\(_3\), TMS): \(\delta 221.7, 173.0, 167.0, 144.1, 136.1, 134.2, 128.7, 127.3, 126.5, 78.5, 53.5, 52.5, 51.7, 39.7, 38.9, 38.1, 36.1, 18.9\) ppm; \(\text{IR}\) (thin film): \(\nu 3434, 2952, 2914, 1722, 1596, 1493, 1435, 1269, 1223, 1163, 1067\); \(\text{HRMS (EI)}\): [C\(_{20}\)H\(_{22}\)O\(_6\)]\(^+\), Calc: 358.1416, Found: 358.1420.

6-tert-Butyl 9-methyl 6-hydroxy-1-oxo-8-phenylspiro[4.5]dec-9-ene-6,9-dicarboxylate (4b)

\[
\begin{align*}
&\text{O} \\
&\text{CO}_2\text{Me} \\
&\text{Ph} \\
&\text{HO} \\
&\text{CO}_2\text{t-Bu}
\end{align*}
\]

Prepared according to general procedure with n-hexane/acetone 10:1 as an eluent to afford 4b (110 mg, 92 %) as a pale sticky oil; \(^1\text{H NMR}\) (400 MHz, CDCl\(_3\), TMS): \(\delta 7.30–7.27\) (m, 2H), 7.21–7.17 (m, 1H), 7.14–7.12 (m, 2H), 6.71 (s, 1H), 5.27 (s, 1H), 4.05 (t, \(J = 8.8\) Hz, 1H), 3.49 (s, 3H), 2.61 (t, \(J = 7.2\) Hz, 1H), 2.53 (dd, \(J_1 = 6.4\) Hz, \(J_2 = 8.0\) Hz, 1H), 2.22–2.19 (m, 1H), 2.13–2.03 (m, 3H), 1.73–1.66 (m, 1H), 1.44 ppm (s, 9H); \(^1\text{C NMR}\) (100 MHz, CDCl\(_3\), TMS): \(\delta 222.0, 171.4, 166.9, 144.2, 135.9, 134.1, 128.5, 127.1, 126.3, 82.7, 78.9, 53.2, 51.5, 39.7, 38.8, 37.8, 36.1, 27.7, 18.7\) ppm; \(\text{IR}\) (thin film): \(\nu 3396, 3028, 2976, 1720, 1642, 1493, 1452, 1394, 1265, 1225, 1161, 1072\); \(\text{HRMS (EI)}\): [C\(_{23}\)H\(_{28}\)O\(_6\)]\(^+\), Calc: 400.1886, Found: 400.1888.

Dimethyl 6-hydroxy-8-(4-methoxyphenyl)-1-oxospiro[4.5]dec-9-ene-6,9-dicarboxylate (4c)

Prepared according to general procedure with n-hexane/acetone 10:1 as an eluent to afford 4c (110 mg, 95 %) as a white solid, m.p. 143–147 °C (ether/n-hexane); \(^1\text{H NMR}\) (500 MHz, CDCl\(_3\), TMS): \(\delta 7.04–7.03\) (m, 2H), 6.82–6.80 (m, 2H), 6.66 (d, \(J = 1\) Hz, 1H), 5.16 (d, \(J = 2\) Hz, 1H), 4.03 (t, \(J = 8.0\) Hz, 1H), 3.77 (s, 3H), 3.68 (s, 3H), 3.51 (s, 3H), 2.60–2.56 (m, 3H), 2.23–2.18 (m, 1H), 2.11–2.03 (m, 2H), 1.96–1.90 (m, 1H), 1.82–1.77 ppm (m, 1H); \(^1\text{C NMR}\) (125 MHz, CDCl\(_3\), TMS): \(\delta 221.7, 173.0, 167.0, 158.1, 135.9, 135.6, 134.5, 128.2, 116.1, 78.5, 53.5, 51.7, 39.7, 38.9, 38.1, 36.1, 18.9\) ppm; \(\text{IR}\) (thin film): \(\nu 3434, 2952, 2914, 1722, 1596, 1493, 1435, 135.6, 134.5, 128.2, 114.1, 78.5, 53.5, 51.7, 39.7, 38.9, 38.1, 36.1, 18.9\) ppm; \(\text{HRMS (EI)}\): [C\(_{20}\)H\(_{22}\)O\(_6\)]\(^+\), Calc: 358.1416, Found: 358.1420.
55.2, 53.4, 52.4, 51.7, 38.8, 38.7, 38.0, 36.1, 18.9 ppm; IR (KBr): ν 3489, 2966, 2945, 1742, 1730, 1712, 1608, 1509, 1350, 1214, 1178, 1084, 1033; HRMS (EI): [C$_{21}$H$_{24}$O$_7$]+, Calc: 388.1522, Found: 388.1517.

**Dimethyl 8-(4-fluorophenyl)-6-hydroxy-1-oxospiro[4.5]dec-9-ene-6,9-dicarboxylate (4d)**

Prepared according to general procedure with *n*-hexane/acetone 10:1 as an eluent to afford 4d (109 mg, 97 %) as a pale sticky oil; $^1$H NMR (400 MHz, CDCl$_3$, TMS): δ 7.08–7.07 (m, 2H), 6.98–6.94 (m, 2H), 6.70 (s, 1H), 5.17 (s, 1H), 4.09–4.05 (m, 1H), 3.69 (s, 3H), 3.51 (s, 3H), 2.61–2.56 (m, 3H), 2.23–2.17 (m, 1H), 2.12–1.97 (m, 3H), 1.81–1.75 ppm (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$, TMS): δ 221.4, 172.7, 166.6, 162.5 ($^{13}$C-F = 240 Hz), 139.5 ($^{13}$C-F = 2.7 Hz), 136.1, 133.9, 128.5 ($^{13}$C-F = 8.5 Hz), 115.3 ($^{13}$C-F = 21.1 Hz), 78.2, 53.3, 52.3, 51.6, 38.8, 38.7, 37.9, 35.9, 18.8 ppm; IR (thin film): ν 3434, 2954, 2899, 1722, 1645, 1508, 1435, 1270, 1222, 1159, 1069; HRMS (EI): [C$_{20}$H$_{21}$FO$_6$]+, Calc: 376.1322, Found: 376.1324.

**Dimethyl 8-(2-chlorophenyl)-6-hydroxy-1-oxospiro[4.5]dec-9-ene-6,9-dicarboxylate (4e)**

Prepared according to general procedure with *n*-hexane/acetone 10:1 as an eluent to afford 4e (112 mg, 95 %) as a white solid, m.p. 135–138 oC (ether/$n$-hexane); $^1$H NMR (500 MHz, CDCl$_3$, TMS): δ 7.36 (s, 1H), 7.14–7.12 (m, 2H), 6.94 (s, 1H), 6.79 (s, 1H), 5.12 (s, 1H), 4.64 (s, 1H), 3.70 (s, 3H), 3.51 (s, 3H), 2.72 (s, 1H), 2.59–2.56 (m, 2H), 2.20 (s, 1H), 2.08–2.03 (m, 2H), 2.00–1.97 (m, 1H), 1.67–1.66 ppm (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$, TMS): δ 221.3, 172.9, 166.6, 141.7, 137.1, 133.6, 129.7, 127.6, 127.2, 127.0, 78.3, 53.5, 52.4, 51.8, 38.8, 36.1, 35.9, 35.8, 35.7, 18.9 ppm; IR (KBr): ν 3441, 3065, 2954, 1724, 1641, 1474, 1432, 1269, 1227, 1190, 1166, 1071; HRMS (EI): [C$_{20}$H$_{21}$ClO$_6$]+, Calc: 392.1027, Found: 392.1028.

**6-Ethyl 9-methyl 6-hydroxy-1-oxo-8-o-tolylspiro[4.5]dec-9-ene-6,9-dicarboxylate (4f)**

Prepared according to general procedure with *n*-hexane/acetone 10:1 as an eluent to afford 4f (101 mg, 87 %) as a pale sticky oil; $^1$H NMR (400 MHz, CDCl$_3$, TMS): δ 7.15–7.14 (m, 1H), 7.10–7.08 (m, 2H), 6.88 (s, 1H), 6.71 (s, 1H), 5.28 (s, 1H), 4.32 (t, $J$ = 8.0 Hz, 1H), 4.17 (q, $J$ = 6.8 Hz, 2H), 3.49 (s, 3H), 2.62–2.53 (m, 3H), 2.45 (s, 3H), 2.25–2.20 (m, 1H), 2.12–1.99 (m, 3H), 1.70 (t, $J$ = 12 Hz, 1H), 1.26 ppm (t, $J$ = 6.8 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$, TMS): δ 222.1, 172.4, 166.8, 142.3, 135.7, 135.5, 134.8, 130.3, 126.4, 126.2, 125.4, 78.4, 61.6, 53.2, 51.6, 38.8, 36.2, 36.0, 35.0, 19.3, 18.8, 13.9 ppm; IR (thin film): ν 3404, 2975, 2928, 1716, 1634, 1596, 1495, 1431, 1378, 1266, 1089, 1048; HRMS (EI): [C$_{22}$H$_{26}$O$_6$]+, Calc: 386.1729, Found: 386.1731.
6-Ethyl 9-methyl 6-hydroxy-8-(3-nitrophenyl)-1-oxospiro[4.5]dec-9-ene-6,9-dicarboxylate (4g)

Prepared according to general procedure with n-hexane/acetone 8:1 as an eluent to afford 4g (120 mg, 96 %) as a white solid, m.p. 146–150 °C (ether/n-hexane); 1H NMR (500 MHz, CDCl3, TMS): δ 8.09–8.07 (m, 1H), 7.96 (s, 1H), 7.52–7.46 (m, 2H), 6.84 (s, 1H), 5.23 (s, 1H), 4.22–4.15 (m, 3H), 3.53 (s, 3H), 2.64–2.60 (m, 3H), 2.27–2.22 (m, 1H), 2.15–2.01 (m, 1H), 1.80–1.75 (m, 1H), 1.26 ppm (t, J = 7.0 Hz, 3H); 13C NMR (125 MHz, CDCl3, TMS): δ 221.3, 172.1, 166.1, 148.5, 146.5, 137.9, 133.9, 132.5, 129.6, 121.9, 121.7, 78.0, 61.9, 53.4, 51.9, 39.5, 38.9, 37.8, 36.1, 18.9, 14.0 ppm; IR (KBr): ν 3409, 3098, 2977, 2952, 1743, 1713, 1523, 1440, 1349, 1273, 1227, 1068; HRMS (EI): [C21H23NO8]+, Calc: 417.1424, Found: 417.1439.

6-Ethyl 9-methyl 8-(4-chlorophenyl)-6-hydroxy-1-oxospiro[4.5]dec-9-ene-6,9-dicarboxylate (4h)

Prepared according to general procedure with n-hexane/acetone 10:1 as an eluent to afford 4h (114 mg, 94 %) as a pale sticky oil; 1H NMR (400 MHz, CDCl3, TMS): δ 7.28–7.24 (m, 2H), 7.08–7.06 (m, 2H), 6.73 (s, 1H), 5.22 (d, J = 1.2 Hz, 1H), 4.15 (q, J = 7.2 Hz, 2H), 4.08–4.04 (m, 1H), 3.52 (s, 3H), 2.59–2.55 (m, 3H), 2.19–2.00 (m, 4H), 1.77–1.71 (m, 1H), 1.26 ppm (t, J = 7.2 Hz, 3H); 13C NMR (100 MHz, CDCl3, TMS): δ 221.6, 172.2, 166.6, 142.5, 136.5, 133.5, 132.0, 128.7, 128.5, 78.1, 61.7, 53.3, 51.7, 39.0, 38.8, 37.7, 36.0, 18.8, 13.9 ppm; IR (thin film): ν 3424, 2975, 2989, 1722, 1644, 1490, 1435, 1407, 1268, 1222, 1091, 1051; HRMS (EI): [C21H23ClO6]+, Calc: 406.1183, Found: 406.1186.

6-Ethyl 9-methyl 8-(furan-2-yl)-6-hydroxy-1-oxospiro[4.5]dec-9-ene-6,9-dicarboxylate (4i)

Prepared according to general procedure with n-hexane/acetone 10:1 as an eluent to afford 4i (105 mg, 97 %) as a pale sticky oil; 1H NMR (500 MHz, CDCl3, TMS): δ 7.29–7.26 (m, 1H), 6.66–6.65 (m, 1H), 6.27–6.26 (m, 1H), 6.00 (d, J = 3.0 Hz, 1H), 4.81 (s, 1H), 4.25–4.22 (m, 1H), 4.16–4.10 (m, 1H), 4.07–4.00 (m, 1H), 3.63 (s, 3H), 2.63 (q, J = 7.0 Hz, 1H), 2.53 (t, J = 8.0 Hz, 2H), 2.25–2.20 (m, 1H), 2.12–2.05 (m, 2H), 2.03–1.97 (m, 2H), 1.23 ppm (t, J = 7.0 Hz, 3H); 13C NMR (125 MHz, CDCl3, TMS): δ 220.4, 172.5, 166.7, 155.5, 141.0, 136.5, 131.6, 110.3, 105.5, 77.5, 61.8, 53.7, 51.8, 39.0, 35.2, 34.3, 33.2, 18.9, 13.9 ppm; IR (thin film): ν 3430, 2974, 2938, 1728, 1441, 1381, 1269, 1084, 1053; HRMS (EI): [C19H22O7]+, Calc: 362.1366, Found: 362.1361.
6-Ethyl 9-methyl 6-hydroxy-1-oxo-8-propylspiro[4.5]dec-9-ene-6,9-dicarboxylate (4j)

Prepared according to general procedure with n-hexane/acetone 15:1 as an eluent to afford 4j (88 mg, 87 %) as a pale sticky oil; 1H NMR (500 MHz, CDCl3, TMS): δ 6.46 (d, J = 1.5 Hz, 1H), 4.89 (d, J = 1.5 Hz, 1H), 4.22-4.17 (m, 2H), 3.74 (s, 3H), 2.89-2.87 (m, 1H), 2.53–2.49 (m, 2H), 2.41 (q, J = 7.0 Hz 1H), 2.04–1.92 (m, 4H), 1.68–1.57 (m, 2H), 1.36–1.28 (m, 6H), 0.91 ppm (t, J = 7.0 Hz, 3H); 13C NMR (125 MHz, CDCl3, TMS): δ 219.1, 170.4, 164.9, 133.2, 132.0, 75.5, 59.1, 51.0, 49.2, 36.3, 33.2, 33.1, 30.7, 29.5, 17.0, 16.3, 11.6, 11.5 ppm; IR (thin film): ν 3439, 2959, 2872, 1732, 1642, 1435, 1403, 1262, 1191, 1129, 1073; HRMS (EI): [C18H26O6]⁺, Calc: 338.1729, Found: 338.1721.

6-Ethyl 9-methyl 8-cyclopropyl-6-hydroxy-1-oxospiro[4.5]dec-9-ene-6,9-dicarboxylate (4k)

Prepared according to general procedure with n-hexane/acetone 15:1 as an eluent to afford 4k (76 mg, 75 %) as a pale sticky oil; 1H NMR (500 MHz, CDCl3, TMS): δ 6.31 (d, J = 1.0 Hz, 1H), 4.82 (d, J = 1.5 Hz,1H), 4.24–4.17 (m, 2H), 3.76 (s, 3H), 2.50 (t, J = 7.5 Hz, 2H), 2.43 (q, J = 7.0 Hz, 1H), 2.27–2.23 (m, 1H), 2.10–1.93 (m, 4H), 1.69–1.64 (m, 1H), 1.29 (t, J = 7.0 Hz, 3H), 0.62-0.58 (m, 1H), 0.54–0.50 (m, 2H), 0.43–0.39 (m, 1H), 0.16–0.13 ppm (m, 1H); 13C NMR (125 MHz, CDCl3, TMS): δ 218.8, 170.6, 166.0, 133.9, 130.7, 75.6, 59.3, 51.3, 49.3, 36.6, 34.2, 33.2, 31.8, 16.5, 13.0, 11.7, 3.7 ppm; IR (thin film): ν 3444, 2977, 2899, 1731, 1642, 1435, 1403, 1264, 1191, 1157, 1045; HRMS (EI): [C18H24O6]⁺, Calc: 336.1573, Found: 336.1576.

9-tert-Butyl 6-methyl 6-hydroxy-1-oxo-8-phenylspiro[4.5]dec-9-ene-6,9-dicarboxylate (4l)

Prepared according to general procedure with n-hexane/acetone 10:1 as an eluent to afford 4l (97 mg, 81 %) as a white solid, m.p. 148–152 °C (ether/n-hexane); 1H NMR (500 MHz, CDCl3, TMS): δ 7.29–7.26 (m, 2H), 7.21–7.18 (m, 1H), 7.13–7.11 (m, 2H), 6.62 (d, J = 2 Hz, 1H), 5.36 (d, J = 2 Hz,1H), 4.01–3.98 (m, 1H), 3.70 (s, 3H), 2.60–2.53 (m, 3H), 2.21–2.17 (m, 1H), 2.10–1.94 (m, 3H), 1.80–1.75 (m, 1H), 1.10 ppm (s, 9H); 13C NMR (125 MHz, CDCl3, TMS): δ 222.1, 173.0, 166.1, 144.5, 135.8, 134.5, 128.5, 127.4, 126.3, 81.0, 78.5, 53.3, 52.4, 39.9, 38.8, 38.0, 36.2, 27.5, 18.8 ppm; IR (KBr): ν 3456, 2985, 2935, 1745, 1705, 1647, 1453, 1437, 1369, 1285, 1239, 1159, 1115, 1068; HRMS (EI): [C23H28O6]⁺, Calc: 400.1886, Found: 400.1891.
Dimethyl 1-hydroxy-7-oxo-3-phenylspiro[5.5]undec-4-ene-1,4-dicarboxylate (4m)

Prepared according to general procedure with n-hexane/acetone 10:1 as an eluent to afford 4m (81 mg, 73 %) from the corresponding propanoate mixtures (60.0 mg, 0.33 mmol) as a white solid, m.p. 130–133 °C (ether/n-hexane); 

\[ ^1H\text{ NMR} \] (400 MHz, CDCl₃, TMS): \( \delta \) 7.30–7.27 (m, 2H), 7.21–7.18 (m, 1H), 7.14–7.13 (m, 3H), 5.55 (d, \( J = 2 \) Hz, 1H), 4.10–4.05 (m, 1H), 3.73 (s, 3H), 3.51 (s, 3H), 2.84–2.76 (m, 1H), 2.58–2.54 (m, 1H), 2.40–2.35 (m, 1H), 2.15–2.14 (m, 3H), 2.01–1.94 (m, 2H), 1.86–1.80 ppm (m, 2H); 

\[ ^{13}C\text{ NMR} \] (100 MHz, CDCl₃, TMS): \( \delta \) 215.1, 173.4, 166.9, 144.0, 138.0, 134.3, 128.6, 126.9, 126.3, 78.5, 55.9, 52.4, 51.6, 39.6, 39.4, 39.1, 37.5, 25.7, 21.0 ppm; 


Product 4m was obtained from the propanoate mixtures (81.9 mg, 0.45 mmol, 1.5 equiv) in 75 % yield (84 mg).

1-Ethyl 4-methyl 3-(furan-2-yl)-1-hydroxy-7-oxospiro[5.6]dodec-4-ene-1,4-dicarboxylate (4n)

Prepared according to general procedure with n-hexane/acetone 10:1 as an eluent to afford 4n (81 mg, 69 %) as a white solid, m.p. 133–136 °C (ether/n-hexane); 

\[ ^1H\text{ NMR} \] (500 MHz, CDCl₃, TMS): \( \delta \) 7.28–7.27 (m, 1H), 6.95–6.94 (m, 1H), 6.28–6.27 (m, 1H), 6.03 (d, \( J = 3.0 \) Hz, 1H), 4.25–4.15 (m, 4H), 3.64 (s, 3H), 2.67–2.64 (m, 2H), 2.41–2.36 (m, 1H), 2.28 (q, \( J = 7.5 \) Hz 1H), 2.15–2.03 (m, 2H), 1.91–1.74 (m, 3H), 1.61–1.47 (m, 3H), 1.29 ppm (t, \( J = 7.0 \) Hz, 3H); 

\[ ^{13}C\text{ NMR} \] (125 MHz, CDCl₃, TMS): \( \delta \) 215.4, 173.2, 166.7, 155.7, 141.1, 139.5, 131.1, 110.3, 105.4, 77.3, 62.1, 58.8, 51.8, 43.2, 34.8, 34.2, 32.8, 30.2, 26.1, 24.8, 14.1 ppm; IR (KBr): \( \nu \) 3422, 2976, 2935, 1722, 1439, 1369, 1266, 1088, 1049; HRMS (EI): [C₂₁H₂₆O₇]⁺, Calc: 390.1679, Found: 390.1682.

Ethyl 4-methyl 3-cyclopropyl-1-hydroxy-7-oxospiro[5.6]dodec-4-ene-1,4-dicarboxylate (4o)

Prepared according to general procedure with n-hexane/acetone 15:1 as an eluent to afford 4o (77 mg, 71 %) as a pale sticky oil; 

\[ ^1H\text{ NMR} \] (500 MHz, CDCl₃, TMS): \( \delta \) 6.60 (s, 1H), 4.28–4.23 (m, 2H), 4.19 (s, 1H), 3.76 (s, 3H), 2.64–2.60 (m, 2H), 2.21–2.14 (m, 1H), 2.10–2.00 (m, 3H), 1.90–1.85 (m, 2H), 1.80–1.78 (m, 1H), 1.70–1.67 (m, 1H), 1.59–1.47 (m, 3H), 1.32 (t, \( J = 7.0 \) Hz, 3H), 0.62–0.59 (m, 1H), 0.54–0.51 (m, 2H), 0.43–0.39 (m, 1H), 0.14–0.11 ppm (m, 1H); 

\[ ^{13}C\text{ NMR} \] (125 MHz, CDCl₃, TMS): \( \delta \) 213.5, 171.4, 166.2, 133.6, 75.3, 59.7, 56.5, 49.4, 40.9, 33.7, 32.9, 31.7, 28.0, 23.8, 22.6, 13.5, 11.9, 3.6 ppm; IR (thin film): \( \nu \) 3497, 2979, 2934, 1720, 1715, 1438, 1366, 1259, 1155, 1117, 1045; HRMS (EI): [C₂₀H₂₆O₅]⁺, Calc: 364.1886, Found: 364.1889.
Diethyl 4-(4-chlorophenyl)-6-hydroxy-1'-oxo-3',4'-dihydro-1'H-spiro[cyclohex[2]ene-1,2'-naphthalene]-3,6-dicarboxylate (4p)

Prepared according to general procedure with n-hexane/acetone 10:1 as an eluent to afford 4p (128 mg, 89 %) as a white solid, m.p. 145–148 °C (ether/n-hexane); ^1H NMR (400 MHz, CDCl₃, TMS): δ 8.13–8.11 (d, J = 8 Hz, 1H), 7.60–7.56 (m, 1H), 7.42–7.38 (m, 1H), 7.32–7.27 (m, 3H), 7.13–7.11 (m, 2H), 6.91 (d, J = 1.6 Hz, 1H), 6.71 (d, J = 2.4 Hz, 1H), 4.17–4.07 (m, 3H), 4.02–3.85 (m, 2H), 3.37–3.28 (m, 1H), 2.98–2.93 (m, 1H), 2.47 (dd, J₁ = 6.8 Hz, J₂ = 8.4 Hz 1H), 2.36–2.22 (m, 2H), 2.06–2.00 (m, 1H), 0.88 ppm (t, J = 7.2 Hz, 3H); ^13C NMR (100 MHz, CDCl₃, TMS): δ 201.7, 172.4, 166.2, 143.2, 142.9, 136.0, 135.9, 134.5, 132.0, 131.3, 128.7, 128.6, 128.5, 127.3, 78.9, 61.4, 60.6, 50.3, 39.4, 36.9, 35.0, 25.4, 13.8, 13.7 ppm; IR (KBr): ν 3373, 2976, 2937, 1720, 1660, 1598, 1549, 1489, 1455, 1409, 1363, 1226, 1093, 1046; HRMS (EI): [C₂₇H₂₇ClO₆]⁺, Calc: 482.1496, Found: 482.1498.

Diethyl 6-hydroxy-1'-oxo-4-propyl-3',4'-dihydro-1'H-spiro[cyclohex[2]ene-1,2'-naphthalene]-3,6-di-carboxylate (4q)

Prepared according to general procedure with n-hexane/acetone 15:1 as an eluent to afford 4q (92 mg, 74 %) as a pale sticky oil; ^1H NMR (400 MHz, CDCl₃, TMS): δ 8.08 (d, J = 7.6 Hz, 1H), 7.55 (t, J = 7.2 Hz, 1H), 7.37 (t, J = 7.6 Hz, 1H), 7.28–7.26 (m, 1H), 6.63 (s, 1H), 6.39 (d, J = 2.4 Hz, 1H), 4.21–4.15 (m, 2H), 4.10 (q, J = 7.2 Hz, 2H), 3.17–3.13 (m, 1H), 2.99–2.97 (m, 1H), 2.87–2.83 (m, 1H), 2.34–2.22 (m, 2H), 2.11–2.06 (m, 1H), 0.94 ppm (t, J = 7.2 Hz, 3H); ^13C NMR (100 MHz, CDCl₃, TMS): δ 202.3, 173.0, 167.0, 143.4, 138.1, 134.3, 133.7, 131.5, 128.5, 128.4, 127.1, 78.9, 61.2, 60.6, 50.3, 39.4, 36.9, 35.0, 25.4, 19.4, 14.1, 14.0, 13.8 ppm; IR (thin film): ν 3366, 2958, 1735, 1729, 1660, 1598, 1489, 1455, 1409, 1363, 1226, 1093, 1046; HRMS (EI): [C₂₄H₃₀O₆]⁺, Calc: 414.2042, Found: 414.2044.

9-((1S,2R,5R)-5-isopropyl-2-methylcyclohexyl)6-methyl8-(4-fluorophenyl)-6-hydroxy-1-oxospino[4.5]dec-9-ene-6,9-dicarboxylate (6)

Prepared according to general procedure with n-hexane/acetone 25:1 as an eluent to afford 6 (142 mg, 95 %) as a
pale sticky oil (d. r. = 3:1); For major diastereomer: \[^1H \text{NMR} \ (400 \text{ MHz, CDCl}_3, \text{TMS}): \delta \ 7.09-7.05 \ (m, 2H), 6.97-6.91 \ (m, 2H), 6.73 \ (s, 1H), 5.22 \ (s, 1H), 4.61-4.55 \ (m, 1H), 4.07-4.03 \ (m, 1H), 3.69 \ (s, 3H), 2.58-2.54 \ (m, 3H), 2.18-2.13 \ (m, 1H), 2.09-1.95 \ (m, 3H), 1.86-1.41 \ (m, 6H), 1.04-0.69 \ (m, 8H), 0.62-0.55 \ (m, 3H), 0.41-0.40 \ ppm \ (m, 2H); \[^{13}C \text{NMR} \ (100 \text{ MHz, CDCl}_3, \text{TMS}): \delta \ 221.5, 172.8, 166.4, 162.6 (J_{C,F} = 242.8 \text{ Hz}), 140.1, 136.2, 134.1, 128.4 (J_{C,F} = 7.4 \text{ Hz}), 115.5 (J_{C,F} = 20.1 \text{ Hz}), 78.2, 74.8, 53.3, 52.3, 46.6, 40.7, 38.7, 38.6, 38.4, 35.9, 33.9, 31.3, 24.6, 22.4, 21.8, 20.9, 18.7, 15.1 \text{ ppm}; \ IR \ (\text{thin film}): \nu \ 3440, 2952, 1732, 1709, 1640, 1506, 1450, 1262, 1221, 1185, 1063; \ HRMS (EI): [C_{29}H_{37}FO_6]^+; \text{Calc:} \ 500.2574, \text{Found:} \ 500.2578.

Methyl 8-(4-chlorophenyl)-10-hydroxy-1-oxo-10-(trifluoromethyl)spiro[4.5]dec-6-ene-7-carboxylate (8)

Prepared according to general procedure with \(n\)-hexane/aceton 20:1 as an eluent to afford 8 (67 mg, 56 %) as a white solid, m. p. 146–148 °C (ether/\(n\)-hexane); \[^1H \text{NMR} \ (400 \text{ MHz, CDCl}_3, \text{TMS}): \delta \ 7.27-7.26 \ (m, 2H), 7.08-7.06 \ (m, 2H), 6.69 \ (s, 1H), 5.77 \ (s, 1H), 4.09-4.05 \ (m, 1H), 3.52 \ (s, 3H), 2.70-2.47 \ (m, 3H), 2.38-2.33 \ (m, 1H), 2.25-2.09 \ (m, 3H), 1.71-1.64 ppm \ (m, 1H); \[^{13}C \text{NMR} \ (100 \text{ MHz, CDCl}_3, \text{TMS}): \delta \ 221.7, 166.3, 141.7, 135.5, 133.6, 132.3, 128.9, 128.4, 127.3, 124.4, 123.9, 123.5, 135.5, 133.6, 128.9, 128.4, 127.3, 124.4, 76.4, 51.9, 51.8, 38.4, 38.3, 35.7, 35.4, 18.5 \text{ ppm}; \ IR \ (\text{KBr}): \nu \ 3361, 2966, 1720, 1650, 1491, 1432, 1273, 1245, 1160, 1123, 1102, 1013; \ HRMS (EI): [C_{19}H_{18}ClF_3O_4]^+; \text{Calc:} \ 402.0846, \text{Found:} \ 402.0845.

Methyl 2-oxo-6-(2-oxocyclopentylidene)-4,5-diphenylhexanoate (11)

Prepared according to the general procedure with \(n\)-hexane/acetone 5:1 as an eluent to afford 11 (67 mg, 61 %) as a colorless oil; \[^1H \text{NMR} \ (500 \text{ MHz, CDCl}_3, \text{TMS): \delta \ 7.17-7.11 \ (m, 4H), 7.10-7.06 \ (m, 2H), 7.03-7.00 \ (m, 4H), 6.79 \ (d, J = 10.5 \text{ Hz}, 1H), 3.75 \ (s, 3H), 3.74-3.67 \ (m, 2H), 3.35 \ (dd, J_1 = 9.0 \text{ Hz}, J_2 = 17.5 \text{ Hz}, 1H), 3.17 \ (dd, J_1 = 4.5 \text{ Hz}, J_2 = 18.0 \text{ Hz}, 1H), 2.57-2.53 \ (m, 2H), 2.36-2.26 \ (m, 2H), 1.93-1.87 \text{ ppm}; \ IR \ (\text{KBr}): \nu \ 3361, 2966, 1720, 1650, 1491, 1432, 1273, 1245, 1160, 1123, 1102, 1013; \ HRMS (EI): [C_{10}H_{18}ClF_3O_4]^+; \text{Calc:} \ 402.0846, \text{Found:} \ 402.0845.

Reference

$^1$H NMR and $^{13}$C NMR spectra

Methyl 3-(2-oxocyclopentylidene)propanoate (1a)

$^1$H-1H COSY
Methyl 3-(2-oxocyclopentylidene)propanoate (1a) $^1$H-$^1$H NOESY

Methyl 3-(2-oxocyclohexylidene)propanoate (keto-A)
Methyl 3-(2-oxocycloheptylidene)propanoate

\[ \text{CO}_2\text{Me} \]

\[ \text{O} \]

\[ \text{CO}_2\text{Me} \]
Ethyl 3-(1-oxo-3,4-dihydronaphthalen-2(1H)-ylidene)propanoate
(()$_{1S,2R,5R}$)-5-isopropyl-2-methylcyclohexyl 3-(2-oxocyclopentylidene)propanoate (5)
2-(2-Phenylethylidene)cyclopentanone (9)
2-Butylidencyclopentanone (10)

[Image of a structural diagram and a spectrum graph]
Dimethyl 5-oxo-2-((2-oxocyclopentylidene)methyl)-3-phenylhexanedioate (3a)
Dimethyl 6-hydroxy-1-oxo-8-phenylspiro[4.5]dec-9-ene-6,9-dicarboxylate (4a)
6-tert-Butyl 9-methyl 6-hydroxy-1-oxo-8-phenylspiro[4.5]dec-9-ene-6,9-dicarboxylate (4b)
Dimethyl 6-hydroxy-8-(4-methoxyphenyl)-1-oxospiro[4.5]dec-9-ene-6,9-dicarboxylate (4c)
Dimethyl 8-(4-fluorophenyl)-6-hydroxy-1-oxospiro[4.5]dec-9-ene-6,9-dicarboxylate (4d)
Dimethyl 8-(2-chlorophenyl)-6-hydroxy-1-oxo[4.5]dec-9-ene-6,9-dicarboxylate (4e)

Electronic Supplementary Material (ESI) for Chemical Communications
This journal is © The Royal Society of Chemistry 2013
6-Ethyl 9-methyl 6-hydroxy-1-oxo-8-o-tolylspiro[4.5]dec-9-ene-6,9-dicarboxylate (4f)
6-Ethyl 9-methyl 6-hydroxy-8-(3-nitrophenyl)-1-oxospiro[4.5]dec-9-ene-6,9-dicarboxylate (4g)
6-Ethyl 9-methyl 8-(4-chlorophenyl)-6-hydroxy-1-oxo[4.5]dec-9-ene-6,9-dicarboxylate (4h)
6-Ethyl 9-methyl 8-(furan-2-yl)-6-hydroxy-1-oxospiro[4.5]dec-9-ene-6,9-dicarboxylate (4i)
6-Ethyl 9-methyl 6-hydroxy-1-oxo-8-propylspiro[4.5]dec-9-ene-6,9-dicarboxylate (4j)
6-Ethyl 9-methyl 8-cyclopropyl-6-hydroxy-1-oxospiro[4.5]dec-9-ene-6,9-dicarboxylate (4k)
9-tert-Butyl 6-methyl 6-hydroxy-1-oxo-8-phenylspiro[4.5]dec-9-ene-6,9-dicarboxylate (4l)
Dimethyl 1-hydroxy-7-oxo-3-phenylspiro[5.5]undec-4-ene-1,4-dicarboxylate (4m)
1-Ethyl 4-methyl 3-(furan-2-yl)-1-hydroxy-7-oxospiro[5.6]dodec-4-ene-1,4-dicarboxylate (4n)
Ethyl 4-methyl 3-cyclopropyl-1-hydroxy-7-oxo[5.6]dodec-4-ene-1,4-dicarboxylate (4o)
Diethyl 4-(4-chlorophenyl)-6-hydroxy-1′-oxo-3′,4′-dihydro-1'H-spiro[cyclohex[2]ene-1,2′-naphthalene]-3,6-
dicarboxylate (4p)
Diethyl 6-hydroxy-1'-oxo-4-propyl-3',4'-dihydro-1'H-spiro[cyclohex[2]ene-1,2'-naphthalene]-3,6-Dicarboxylate (4q)
9-((1S,2R,5R)-5-isopropyl-2-methylcyclohexyl)6-methyl-8-(4-fluorophenyl)-6-hydroxy-1-oxospiro[4.5]dec-9-ene-6,9-dicarboxylate (6)
Methyl 8-(4-chlorophenyl)-10-hydroxy-1-oxo-10-(trifluoromethyl)spiro[4.5]dec-6-ene-7-carboxylate (8)
Methyl 2-oxo-6-(2-oxocyclopentylidene)-4,5-diphenylhexanoate (11)