Synthesis of chiloglottones – semiochemicals from sexually deceptive orchids and their pollinators

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Representative Procedure for preparation of 2. Reductive alkylations were performed with adaptations to published procedures.\textsuperscript{1,2} To a solution of 3,5-dimethoxybenzoic acid (1 equiv.) in dry THF (2 mL/mmol) liquid NH\textsubscript{3} (approx. 5 mL/mmol) was condensed. Lithium (2.2 equiv.) was added in portions at -33°C until a deep blue color persisted. The appropriate alkyl halide (1.2 equiv.) was added dropwise, causing an immediate reversion of the color change through orange to colorless. NH\textsubscript{3} was evaporated under a stream of N\textsubscript{2} overnight. The residue was partitioned between Et\textsubscript{2}O and H\textsubscript{2}O, the aqueous layer chilled to 0°C and acidified to pH 3-4 with careful addition of 2N HCl. The aqueous layer was reextracted (EtOAc), the organic phase washed (H\textsubscript{2}O), dried (MgSO\textsubscript{4}) and concentrated in vacuo. The solid residue was recrystallized from CH\textsubscript{2}Cl\textsubscript{2} to return the diene acid 2.

3,5-dimethoxy-1-methylcyclohexa-2,5-dienecarboxylic acid (2b)

\begin{center}
\includegraphics[width=0.2\textwidth]{image1}
\end{center}

Yield = 79% as colorless prisms. IR (neat): br. 3430, 1724, 1600 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): \(\delta\) 4.71 (2H, dd, \(^4J = 1.5, ^4J = 1.5\), H-2,6), 3.59 (6H, s, 3,5–O\textsubscript{CH\textsubscript{3}}), 2.82 (1H, dt, \(^2J = 20.7, ^4J = 1.5\), H-4a), 2.73 (1H, dt, \(^2J = 20.7, ^4J = 1.5\), H-4b), 1.41 (3H, s, H-1'); \textsuperscript{13}C APT NMR (75 MHz, CDCl\textsubscript{3}): \(\delta\) 172.2 (C, 1-C\textsubscript{O\textsubscript{2}H}), 152.7 (C, C-3,5), 96.4 (CH, C-2,6), 54.4 (CH\textsubscript{3}, 3,5–O\textsubscript{CH\textsubscript{3}}), 45.8 (C, C-1), 30.9 (CH\textsubscript{2}, C-4), 29.0 (CH\textsubscript{3}, C-1'); \textit{m/z} (ESI) 199.0963 [(M+H)+C\textsubscript{10}H\textsubscript{15}O\textsubscript{4} requires 199.0970 (\(\Delta = 3.6\) ppm)].

3,5-dimethoxy-1-ethylcyclohexa-2,5-dienecarboxylic acid (2c)

\begin{center}
\includegraphics[width=0.2\textwidth]{image2}
\end{center}

Yield = 78% as colorless prisms. IR (neat): v. br. 3400, 2090, 1640 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): \(\delta\) 4.65 (2H, dd, \(^4J = 1.2, ^4J = 1.2\), H-2,6), 3.60 (6H, s, 3,5–O\textsubscript{CH\textsubscript{3}}), 2.77-2.66 (2H, m, H-4), 1.75 (2H, q,
3J = 7.5, H-1'), 0.82 (3H, t, 3J = 7.5, H-2'); 13C APT NMR (75 MHz, CDCl3): δ 182.5 (C, 1-CO2H), 153.4 (C, C-3,5), 94.4 (CH, C-2,6), 54.4 (CH3, 3,5–OCH3), 50.3 (C, C-1), 33.7 (CH2, C-1'), 31.1 (CH2, C-4), 8.6 (CH3, C-2'); m/z (ESI) 213.1121 [(M+H)+ C11H17O4 requires 213.1127 (Δ = 2.8 ppm)].

3,5-dimethoxy-1-propylcyclohexa-2,5-dienecarboxylic acid (2d)

![Structure image]

Yield = 99% as colorless prisms. IR (neat): v. br. 3400, 2090, 1643 cm⁻¹; 1H NMR (300 MHz, CDCl3): δ 4.68 (2H, s, H-2,6), 3.60 (6H, s, 3,5–OCH3), 2.75 (2H, s, H-4), 1.73-1.67 (2H, m, H-1'), 1.31-1.20 (2H, m, H-2'), 0.90 (3H, t, 3J = 7.2, H-3'); 13C APT NMR (75 MHz, CDCl3): δ 182.8 (C, CO2H), 153.0 (C, C-3,5), 94.8 (CH, C-2,6), 54.4 (CH3, 3,5–OCH3), 49.9 (C, C-1), 43.4 (CH2, C-1'), 31.1 (CH2, C-4), 17.6 (CH2, C-2'), 14.2 (CH3, C-3'); m/z (ESI) 227.1289 [(M+H)+ C12H19O4 requires 227.1283 (Δ = 2.8 ppm)].

3,5-dimethoxy-1-butylcyclohexa-2,5-dienecarboxylic acid (2e)

![Structure image]

Yield = 77% as colorless prisms. IR (neat): v. br. 3400, 2090, 1640 cm⁻¹; 1H NMR (300 MHz, CDCl3): δ 4.68 (2H, s, H-2,6), 3.60 (6H, s, 3,5–OCH3), 2.76 (2H, s, H-4), 1.74-1.68 (2H, m, H-1'), 1.32-1.16 (4H, m, H-2' and H-3'), 1.70 (3H, t, 4J = 7.2, H-4'); 13C APT NMR (75 MHz, CDCl3): δ 182.8 (C, CO2H), 153.1 (C, C-3,5), 94.9 (CH, C-2,6), 54.4 (CH3, 3,5–OCH3), 49.9 (C, C-1), 40.9 (CH2, C-1'), 31.1 (CH2, C-4), 26.4 (CH2, C-2'), 22.9 (CH2, C-3'), 14.0 (CH3, C-4'); m/z (ESI) 241.1437 [(M+H)+ C13H21O4 requires 241.1440 (Δ = 1.2 ppm)].
3,5-dimethoxy-1-pentylcyclohexa-2,5-dienecarboxylic acid (2f)

Yield = 44% as colorless prisms. IR (neat): v. br. 3400, 2090, 1643 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): \( \delta \) 4.67 (2H, s, H-2,6), 3.60 (6H, s, 3,5–OCH₃), 2.76 (2H, s, H-4), 1.73-1.68 (2H, m, H-1'), 1.32-1.15 (6H, m, H-2', H-3' and H-4'), 0.86 (3H, t, \( ^3J = 7.2 \), H-5'); ¹³C APT NMR (75 MHz, CDCl₃): \( \delta \) 182.8 (C, 1-CO₂H), 153.1 (C, C-3,5), 94.9 (CH, C-2,6), 54.4 (CH₃, 3,5–OCH₃), 49.9 (C, C-1), 41.0 (CH₂, C-1'), 32.0 (CH₂, C-3'), 31.1 (CH₂, C-4), 23.9 and 22.5 (CH₂, C-2' and C-4'), 14.0 (CH₃, C-5'); m/z (ESI) 255.1596 [(M+H)+ C₁₄H₂₃O₄ requires 255.1596 (\( \Delta = 0.0 \) ppm)].

Representative Procedure for synthesis of 3: Following a published account with minor modifications;¹ to a rapidly stirred solution of 2 (1 equiv.) in benzene (20 mL/mmol) was added Pb(OAc)₄ (1.3 equiv.). After 30-40 min, by which time the mixture had become colorless, H₂O (approx. equivolume to benzene) was added and the mixture filtered under vacuum through a plug of silica. The aqueous phase was extracted with Et₂O and the combined organic extracts washed (sat. aqueous NaHCO₃ solution), dried (MgSO₄) and the solvents removed in vacuo to give 3 as a pale mobile oil.

1,3-dimethoxy-5-methylbenzene (3b)
Yield = 91% as pale yellow oil: IR (neat): 2997, 2940, 2835, s. 1597, 1462, 1204, 1150, 829 cm⁻¹; ¹H NMR: (300 MHz, CDCl₃): δ 6.35 (2H, d, ⁴J = 2.1, H-4,6), 6.30 (1H, t, ⁴J = 2.1, H-2), 3.78 (6H, s, 1,3–OCH₃), 2.31 (3H, s, H-1'); ¹³C NMR: (75 MHz, CDCl₃): δ 160.7 (C, C-1,3), 140.2 (C, C-5), 107.0 (CH, C-4,6), 97.5 (CH, C-2), 55.2 (CH₃, 1,3–OCH₃), 21.8 (CH₃, C-1'); m/z (EI) 152.0833 [M⁺• C₉H₁₂O₂ requires 152.0837 (Δ = 2.8 ppm)].

1,3-dimethoxy-5-ethylbenzene (3c)

Yield = 94% as pale yellow oil: IR (neat): 2997, 2943, 2835, s. 1598, 1462, 1204, 1145, 829 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 6.37 (2H, d, ⁴J = 2.1, H-4,6), 6.30 (1H, t, ⁴J = 2.1, H-2), 3.79 (6H, s, 1,3–OCH₃), 2.60 (2H, q, ³J = 7.5, H-1'), 1.23 (3H, t, ³J = 7.5, H-2'); ¹³C APT NMR (75 MHz, CDCl₃): δ 160.7 (C, C-1,3), 146.7 (C, C-5), 105.9 (CH, C-4,6), 97.5 (CH, C-2), 55.2 (CH₃, 1,3–OCH₃), 29.2 (CH₂, C-1'), 15.4 (CH₃, C-2'); m/z (EI) 166.0992 [M⁺• C₁₀H₁₄O₂ requires 166.0994 (Δ = 1.1 ppm)].

1,3-dimethoxy-5-propylbenzene (3d)

Yield = 99% as a pale yellow oil: IR (neat): 2997, 2959, 2832, s. 1597, 1462, 1204, 1150, 829 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 6.35 (2H, d, ⁴J = 2.1, H-4,6), 6.30 (1H, t, ⁴J = 2.1, H-2), 3.78 (6H, s, 1,3–OCH₃), 2.53 (2H, t, ³J = 7.5, H-1'), 1.63 (2H, tq, ³J = 7.5, ³J = 7.5, H-2'), 1.23 (3H, t, ³J = 7.5, H-3'); ¹³C NMR APT NMR (75 MHz, CDCl₃): δ 160.6 (C, C-1,3), 145.1 (C, C-5), 106.5 (CH, C-4,6), 97.5 (CH, C-2), 55.2 (CH₃, 1,3–OCH₃), 38.4 (CH₂, C-1'), 24.3 (CH₂, C-2'), 13.9 (CH₃, C-3'); m/z (EI) 180.1149 [M⁺• C₁₁H₁₆O₂ requires 180.1150 (Δ = 0.7 ppm)].
1,3-dimethoxy-5-butylbenzene (3e)

Yield = 88% as a pale yellow oil: IR (neat): 2995, 2950, 2835, s. 1595, 1462, 1205, 1150, 829 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 6.35 (2H, d, ⁴J = 2.1, H-4,6), 6.30 (1H, t, ⁴J = 2.1, H-2), 3.78 (6H, s, 1,3–OCH₃), 2.55 (2H, t, ³J = 7.5, H-1′), 1.59 (2H, tt, ³J = 7.5, ³J = 7.5, H-2′), 1.23 (2H, tq, ³J = 7.5, ³J = 7.2, H-3′), 0.93 (2H, t, ³J = 7.2, H-4′); ¹³C NMR APT NMR (75 MHz, CDCl₃): δ 160.6 (C, C-1,3), 145.4 (C, C-5), 106.4 (CH, C-4,6), 97.5 (CH, C-2), 55.2 (CH₃, 1,3–OCH₃), 36.0 (CH₂, C-1′), 33.4 (CH₂, C-2′), 22.4 (CH₂, C-3′), 13.9 (CH₃, C-4′); m/z (EI) 194.1307 [M⁺ C₁₂H₁₈O₂ requires 194.1307 (Δ = 0.1 ppm)].

1,3-dimethoxy-5-pentylbenzene (3f)

Yield = 84% as a clear colourless oil: IR (neat): 2997, 2959, 2835, s. 1602, 1462, 1198, 1149, 829 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 6.35 (2H, d, ⁴J = 2.4, H-4,6), 6.30 (1H, t, ⁴J = 2.4, H-2), 3.79 (6H, s, 1,3–OCH₃), 2.55 (2H, t, ³J = 7.5, H-1′), 1.61 (2H, tt, ³J = 7.5, ³J = 7.5, H-2′), 1.35-1.30 (4H, m, H-3′ and H-4′), 0.93 (2H, t, ³J = 7.2, H-5′); ¹³C NMR APT NMR (75 MHz, CDCl₃): δ 160.6 (C, C-1,3), 145.4 (C, C-5), 106.5 (CH, C-4,6), 97.5 (CH, C-2), 55.2 (1,3–OCH₃), 36.3 (CH₂, C-1′), 31.5 and 30.9 (CH₂, C-2′ and C-3′), 22.5 (CH₂, C-4′), 14.0 (CH₃, C-5′); m/z (EI) 208.1460 [M⁺ C₁₃H₂₀O₂ requires 208.1463 (Δ = 1.7 ppm)].
Representative Procedure for preparation of 4: To a solution of 3 (1 equiv.) in dry THF (approx. 4.5 mL/mmol) and tBuOH (approx. 4.5 mL/mmol), NH₃ (approx. 10-15 mL/mmol) was condensed. Lithium (17 equiv.) was added in portions at -33°C and the solution allowed to warm slowly to r.t. NH₃ was evaporated under a stream of N₂ and the residue partitioned between Et₂O and sat. aqueous NH₄Cl solution. The aqueous was reextracted (Et₂O), the combined organics dried (MgSO₄) and concentrated under vacuum to return the diene 4.

1,5-dimethoxy-3-methylcyclohexa-1,4-diene (4b)

Yield = 61% as a pale yellow oil. IR (neat): 3000, 2955, 2865, s. 1600, 1382, 1205, 1150, 825 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 4.57 (2H, ddd, ³J = 3.3, ⁴J = 1.2, ⁴J = 1.2, H-2,4), 3.56 (6H, s, 1,5–OCH₃), 3.04 (1H, qtdd, ³J = 6.9, ³J = 3.3, ⁵J = 6.9, ⁵J = 6.9, H-3), 2.81-2.71 (2H, m, H-6), 1.08 (3H, d, ³J = 6.9 H-1'); ¹³C APT NMR (75 MHz, CDCl₃): δ 151.2 (C, C-1,5), 97.7 (CH, C-2,4), 54.1 (CH₃, 1,5–OCH₃), 31.0 (CH₂, C-6), 30.6 (CH, C-3), 24.5 (CH₃, C-1'); m/z (EI) 154.0994 [M⁺* C₉H₁₄O₂ requires 154.0996 (Δ = 0.1 ppm)].

1,5-dimethoxy-3-ethylcyclohexa-1,4-diene (4c)
Yield = 83% as a clear colourless oil. b.p. 145°C @ 1.5mmHg; IR (neat): 3059, 2997, 2959, 2824, s. 1694, 1663, 1597, 1443, 1397, 1234, 1207, 1150 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 4.58-4.57 (2H, m, H-2,4), 3.57 (6H, s, 1,5-OCH₃), 2.94 (1H, tddd, 3J = 7.0, 3J = 3.3, 5J = 6.6, 5J = 6.6, H-3), 2.77-2.76 (2H, m [apparent d], J = 6.5, H-6), 1.43 (2H, dq, 3J = 7.0, 3J = 7.0, H-1'), 0.87 (3H, t, 3J = 7.0, H-2'); ¹³C APT NMR (75 MHz, CDCl₃): δ 151.9 (C, C-1,5), 65.7 (CH, C-2,4), 54.1 (CH₃, 1,5-OCH₃), 36.8 (C-3), 31.3 (CH₂, C-6), 30.7 (CH₂, C-1'), 10.4 (CH₃, C-2'); m/z (ESI) 169.1226 [(M+H)⁺ C₁₀H₁₇O₂ requires 169.1229 (Δ = 1.7 ppm)].

1,5-dimethoxy-3-propylcyclohexa-1,4-diene (4d)

Yield = 88% as a pale yellow oil. IR (neat): 3059, 2997, 2955, 2870, 2839, s. 1693, 1659, 1609, 1462, 1204, 1150 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 4.60-4.59 (2H, m, H-2,4), 3.56 (6H, s, 1,5-OCH₃), 3.03-2.93 (1H, m, H-3), 2.77-2.75 (2H, m [apparent d], J = 6.9, H-6), 1.37-1.34 (4H, m, H-1' and H-2'), 0.91 (3H, t, 3J = 7.0, H-3'); ¹³C APT NMR (75 MHz, CDCl₃): δ 151.6 (C, C-1,5), 96.0 (CH, C-2,4), 54.1 (CH₃, 1,5-OCH₃), 40.6 (CH₂, C-1'), 35.4 (CH₂, C-3), 31.3 (CH₂, C-6), 19.4 (CH₂, C-2'), 14.3 (CH₃, C-3'); m/z (ESI) 183.1383 [(M+H)⁺ C₁₁H₁₉O₂ requires 183.1385 (Δ = 1.1 ppm)].

1,5-dimethoxy-3-butylcyclohexa-1,4-diene (4e)

Yield = 100% as a pale yellow oil: b.p. 150°C @ 0.7mmHg; IR (neat): 3059, 2997, 2955, 2928, 2855, 1693, 1663, 1609, 1462, 1397, 1207, 1150 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 4.60 (2H, ddd, 3J = 3.3,
$J = 1.2$, $J = 1.2$, $H-2,4$), 3.56 (6H, s, $1,5\text{-OCH}_3$), 3.03-2.91 (1H, $m$, H-3), 2.76 (2H, $m$, H-6) 1.42-1.25 (6H, $m$, H-1', H-2' and H-3'), 0.90 (3H, $t$, $^3J = 7.2$, H-4'); $^{13}$C APT NMR (75 MHz, CDCl$_3$): $\delta$ 151.6 (C, C-1,5), 96.1 (CH, C-2,4), 54.1 (CH$_3$, 1,5–OCH$_3$), 38.1 (CH$_2$, C-1'), 35.6 (CH, C-3), 31.3 (CH$_2$, C-6), 28.5 (CH$_2$, C-2'), 23.0 (CH$_2$, C3'), 14.1 (CH$_3$, C4'); $m/z$ (EI) 196.1463 [M$^{+}$ C$_{12}$H$_{20}$O$_2$ requires 196.1460 ($\Delta = 1.9$ ppm)].

**1,5-dimethoxy-3-pentylcyclohexa-1,4-diene (4f)**

Yield = 85% as a pale yellow oil; IR (neat): 3059, 2997, 2955, 2928, 2870, s. 1695, 1663, 1610, 1443, 1204, 1150 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 4.59 (2H, $d$, $^3J = 3.6$, H-2,4), 3.56 (6H, s, 1,5-OCH$_3$), 2.96 (1H, $ttdd$, $^3J = 7.2$, $^5J = 7.2$, H-3), 2.78-2.75 (2H, $m$, [apparent $d$], $J = 7.2$, H-6) 1.4-1.25 (8H, $m$, H-1', H-2', H-3' and H-4'), 0.89 (3H, $t$, $^3J = 6.9$, H-5'); $^{13}$C APT NMR (75 MHz, CDCl$_3$): $\delta$ 151.6 (C, C-1,5), 96.1 (CH, C-2,4), 54.1 (CH$_3$, 1,5–OCH$_3$), 38.3 (CH$_2$, C-1'), 35.6 (CH, C-3), 31.3 (CH$_2$, C-6), 32.2 and 26.0 (CH$_2$, C-2' and C-3'), 22.7 (CH$_2$, C-4'), 14.1 (CH$_3$, C-5'); $m/z$ (ESI) 211.1696 [(M+H)$^+$ C$_{13}$H$_{23}$O$_2$ requires 211.1698 ($\Delta = 0.9$ ppm)].

**Representative Procedure for preparation of 5:** Alkylations were achieved in a similar manner to previously reported methods.$^3$ A solution of 4 (1 equiv.) in dry THF (10 mL/mm) was cooled to -78°C. tBuLi (1.1 equiv., 1.255 M in pentane) was added dropwise via syringe. The solution was stirred for 30 min at -78°C before dropwise addition of the required alkyl halide (1.6 equiv). After 10-15 min at -78°C the suspension was slowly warmed to r.t. and quenched with H$_2$O. The aqueous residue was
extracted with Et$_2$O, the combined organic phases dried (MgSO$_4$) and the solvents removed in vacuo, returning 5, which was immediately hydrolyzed to 1, without separation of diastereomers.

**Representative Procedure for synthesis of 1:** With modifications on a reported method,$^4$ crude 5 (1 equiv.) was dissolved in acetone (5 mL/mmol) and aq. 2N HCl (3 equiv.) added. The resulting solution was stirred overnight at r.t. The acetone was evaporated under reduced pressure and the residue diluted (H$_2$O), basified (aq. 1N NaOH) and washed with Et$_2$O. The aqueous layer was reacidified (pH 1-3 aq. 2N HCl) and extracted with EtOAc. The organic phase was dried (MgSO$_4$) and concentrated in vacuo to return 1 as a white solid.

**5-propyl-1,3-cyclohexanedione (1da)**

Yield = 88% as spreading colorless crystals: m.p. 95-99°C; IR (neat): br. 3310, 2957, 2930, 2872, br. 2550, 1572, 1232 cm$^{-1}$; $^1$H NMR (500 MHz, CD$_3$OD): $\delta$ 2.40 (2H, d, $^2$J = 12.5, H-4eq, 6eq), 2.12-2.09 (1H, m, H-5), 2.10 (2H, d, $^2$J = 12.5, H-4ax, 6ax), 1.39-1.38 (4H, m, H-1$'$ and H-2$'$), 0.93 (3H, t, $^3$J = 7.0, H-3$'$); $^{13}$C APT NMR (125 MHz, CD$_3$OD): $\delta$ 104.3 (CH, C-2), 39.7 (br, CH$_2$, C-4,6), 38.8 (CH$_2$, C-1$'$), 34.9 (CH, C-5), 20.8 (CH$_2$, C-2$'$), 14.4 (CH$_3$, C-3$'$); m/z (El) 154.0992 [M$^+$ C$_9$H$_{14}$O$_2$ requires 154.0994 ($\Delta = 0.9$ ppm)], 154 (7%), 139 (1), 126 (3), 111 (23), 97 (100), 83 (82), 69 (28), 55 (83).

**2-methyl-5-propyl-1,3-cyclohexanedione (1db)**
Yield = 92% over two steps. m.p. 111-115°C; IR (neat): br. 3060, 2955, 2930, 2872, br. 2650, 1572, 1383, 1242, 1088 cm\(^{-1}\); \(^1\)H NMR (500 MHz, CD\(_3\)OD): \(\delta\) 2.44 (2H, \(dd\), \(^2J = 16.5, \ ^3J = 4.0\), H-4eq, 6eq), 2.13 (2H, \(dd\), \(^2J = 16.5, \ ^3J = 11.0\), H-4ax, 6ax), 2.06-2.01 (1H, \(m\), H-5), 1.63 (3H, \(s\), H-1”), 1.37-1.35 (4H, \(m\), H-1’ and H-2’), 0.92 (3H, \(t\), \(^3J = 7.0\), H-3’); \(^{13}\)C APT NMR (125 MHz, CD\(_3\)OD): \(\delta\) 111.5 (C, C-2), 38.9 (CH\(_2\), C-1’), 34.5 (CH, C-5), 20.7 (CH\(_2\), C-2’), 14.4 (CH\(_3\), C-3’), 7.1 (CH\(_3\), C-1’); \(m/z\) (EI) 168.1151 [M\(^+\)C\(_{10}\)H\(_{16}\)O\(_2\) requires 168.1150 (\(\Delta = 0.3\) ppm)], 168 (25%), 153 (<1), 140 (6), 125 (10), 111 (2), 97 (100), 83 (10), 70 (17), 55 (43).

2-ethyl-5-propyl-1,3-cyclohexanedione “Chiloglottone 1” (1dc)

Yield = 82% over two steps. m.p. 124-126°C; IR (neat): 2957, 2928, 2872, br. 2640, 1557, 1383, 1263, 1244, 1105 cm\(^{-1}\); \(^1\)H NMR (500 MHz, CD\(_3\)OD): \(\delta\) 2.46 (2H, \(dd\), \(^2J = 16.5, \ ^3J = 4.3\), H-4eq, 6eq), 2.25 (2H, \(q\), \(^3J = 7.5\), H-1”), 2.14 (2H, \(dd\), \(^2J = 16.5, \ ^3J = 11.3\), H-4ax, 6ax), 2.07-2.01 (1H, \(m\), H-5), 1.39-1.34 (4H, \(m\), H-1’ and H-2’), 0.94 (3H, \(t\), \(^3J = 6.5\), H-3’), 0.90 (3H, \(t\), \(^3J = 7.5\), H-2’); \(^{13}\)C APT NMR (125 MHz, CD\(_3\)OD): \(\delta\) 176.5 (C, C-1,3), 118.5 (C, C-2), 39.3 (CH\(_2\), C-4,6), 38.8 (CH\(_2\), C-1’), 34.4 (CH, C-5), 20.7 (CH\(_2\), C-2’), 16.0 (CH\(_2\), C-1”), 14.4 and 13.6 (CH\(_3\), C-2”, C-3’); \(m/z\) (EI) 182.1307 [M\(^+\)C\(_{11}\)H\(_{18}\)O\(_2\) requires 182.1307 (\(\Delta = 0.1\) ppm)], 182 (39%), 167 (5), 154 (6), 139 (17), 125 (42), 111 (30), 97 (100), 84 (35), 69 (39), 55 (78).
2,5-dipropyl-1,3-cyclohexanedione (1dd)

\[
\begin{align*}
\text{Yield} &= \text{75\% over two steps. m.p. 133-138^\circ C; IR (neat)}: \text{br. 3425, 2957, 2928, 2872, br. 2640, 1566, 1383, 1240, 1233, 1113 cm}^{-1}; \text{H NMR (500 MHz, CD}_3\text{OD):} \delta 2.44 (2H, dd, ^2J = 14.0, ^3J = 3.0, H-4eq, 6eq), 2.19 (2H, t, ^3J = 7.5, H-1'), 2.13 (2H, dd, ^2J = 14.0, ^3J = 11.0, H-4ax, 6ax), 2.06-2.00 (1H, m, H-5), 1.38-1.35 (4H, H-1' and H-2'), 1.33 (2H, tq [apparent hex], ^3J = 7.5, ^3J = 7.0, H-2''), 0.93 (3H, t, ^3J = 7.0, H-3'), 0.85 (3H, t, ^3J = 7.0, H-3''); \text{C APT NMR (125 MHz, CD}_3\text{OD):} \delta 116.6 (C, C-2), 38.9 (CH}_2\text{, C-1'), 34.5 (CH, C-5), 24.7 (CH}_2\text{, C-1''), 22.8 (CH}_2\text{, C-2''), 20.8 (CH}_2\text{, C-2'), 14.43 and 14.38 (CH}_3\text{, C-3' and C-3''); m/z (EI) 196.1457 [M}^+\text{ C}_{12}\text{H}_{20}\text{O}_2 \text{ requires 196.1463 (}\Delta = 3.3 \text{ ppm})], 196 (33\%), 181 (32), 167 (32), 154 (14), 139 (29), 125 (30), 111 (67), 97 (100), 84 (40), 69 (22), 55 (82).
\end{align*}
\]

2-butyl-5-propyl-1,3-cyclohexanedione (1de)

\[
\begin{align*}
\text{Yield} &= \text{81\% over two steps. m.p. 141-146 \degree C; IR (neat):} \text{br. 3050, 2957, 2926, 2872, br. 2621, 1568, 1383, 1242, 1115 cm}^{-1}; \text{H NMR (500 MHz, CD}_3\text{OD):} \delta 2.44 (2H, dd, ^2J = 16.5, ^3J = 4.0, H-4eq, 6eq), 2.21 (2H, t, ^3J = 7.0, H-1'), 2.13 (2H, dd, ^2J = 16.5, ^3J = 11.0, H-4ax, 6ax), 2.06-2.00 (1H, m, H-5), 1.37-1.35 (4H, m, H-1' and H-2'), 1.29-1.26 (4H, m, H-2'' and H-3''), 0.93 (3H, t, ^3J = 7.0, H-3'), 0.88 (3H, t, ^3J = 7.0, H-4''); \text{C APT NMR (125 MHz, CD}_3\text{OD):} \delta 116.8 (C, C-2), 40.5 (br, CH}_2\text{, C-4,6),}
\end{align*}
\]
38.9 (CH₂, C-1′), 34.5 (CH, C-5), 32.0 (CH₂, C-2″), 23.8 (CH₂, C-3″), 22.4 (CH₂, C-1″), 20.8 (CH₂, C-2′), 14.5 and 14.4 (CH₃, C-3′ and C-4″); m/z (EI) 210.1618 [M⁺ C₁₃H₂₂O₂ requires 210.1620 (Δ = 0.6 ppm)], 210 (19%), 195 (6), 181 (38), 167 (34), 155 (28), 139 (27), 125 (37), 111 (56), 97 (100), 84 (37), 69 (25), 55 (67).

2-pentyl-5-propyl-1,3-cyclohexanedione (1df)

Yield = 69% over two steps. m.p. 139-143°C; IR (neat): br. 3450, 2957, 2928, 2872, br. 2633, 1568, 1385, 1242, 1115 cm⁻¹; ¹H NMR (500 MHz, CD₃OD): δ 2.44 (2H, dd, ²J = 16.5, ³J = 3.5, H-4eq, 6eq), 2.20 (2H, t, ³J = 7.0, H-1″), 2.13 (2H, dd, ²J = 16.5, ³J = 11.0, H-4ax, 6ax), 2.05-2.00 (1H, m, H-5), 1.37-1.35 (4H, m, H-1′, and H-2′), 1.32-1.22 (6H, m, H-2″, H-3″ and H-4″), 0.93 (3H, t, ³J = 7.0, H-3′), 0.87 (3H, t, ³J = 7.0, H-5″); ¹³C APT NMR (125 MHz, CD₃OD): δ 116.8 (C, C-2), 38.8 (CH₂, C-1′), 34.5 (CH, C-5), 33.0 (CH₂, C-3″), 29.4 (CH₂, C-2″), 23.7 and 22.6 (CH₂, C-1″ and C-4″), 20.8 (CH₂, C-2′), 14.5 and 14.4 (CH₃, C-3′ and C-5″); m/z (EI) 224.1776 [M⁺ C₁₄H₂₄O₂ requires 224.1776 (Δ = 0.0 ppm)], 224 (17%), 209 (5), 195 (16), 181 (50), 168 (19), 155 (46), 139 (24), 125 (23), 111 (63), 97 (100), 84 (40), 69 (23), 55 (68).

2-hexyl-5-propyl-1,3-cyclohexanedione (1dg)
Yield = 66% over two steps. m.p. 133-136°C; IR (neat): br. 3055, 2957, 2926, 2872, br. 2645, 1568, 1383, 1242, 1117 cm\(^{-1}\); \(^1\)H NMR (500 MHz, CD\(_3\)OD): \(\delta\) 2.44 (2H, \(dd\), \(^2J = 16.5\), \(^3J = 4.0\), H-4eq, 6eq), 2.20 (2H, \(t\), \(^3J = 7.0\), H-1\('\)), 2.13 (2H, \(dd\), \(^2J = 16.5\), \(^3J = 11.0\), H-4ax, 6ax), 2.06-2.00 (1H, \(m\), H-5), 1.37-1.35 (4H, \(m\), H-1\('\) and H-2\('\)), 1.30-1.24 (8H, \(m\), H-2\('\), H-3\('\), H-4\('\) and H-5\('\)), 0.92 (3H, \(t\), \(^3J = 7.0\), H-3\('\)), 0.88 (3H, \(t\), \(^3J = 7.0\), H-6\('\)); \(^{13}\)C APT NMR (125 MHz, CD\(_3\)OD): \(\delta\) 116.8 (C, C-2), 38.8 (CH\(_2\), C-1\('\), 34.5 (CH, C-5), 33.0 and 30.4 (CH\(_2\), C-3\('\) and C-4\('\)), 29.7 (CH\(_2\), C-2\('\)), 23.8 and 22.7 (CH\(_2\), C-1\('\) and C-5\('\)), 20.8 (CH\(_2\), C-2\('\)), 14.5 and 14.4 (CH\(_3\), C-3\('\) and C-6\('\)); \(m/z\) (EI) 238.1936 [M\(^+\) \(\text{C}_{15}\text{H}_{26}\text{O}_2\) requires 238.1933 (\(\Delta = 1.2 \text{ ppm}\))], 238 (31%), 223 (<1), 209 (6), 195 (35), 181 (41), 168 (31), 155 (76), 139 (21), 125 (27), 111 (71), 97 (100), 84 (41), 69 (23), 55 (75).

\textit{2-ethyl-5-pentyl-1,3-cyclohexanedione “Chiloglottone 2” (1fc)}

Yield = 72% over two steps. IR (neat): br. 3448, 2957, 2928, 2872, br. 2639, 1560, 1385, 1242, 1108 cm\(^{-1}\); \(^1\)H NMR (500 MHz, CD\(_3\)OD): \(\delta\) 2.44 (2H, \(dd\), \(^2J = 16.5\), \(^3J = 4.0\), H-4eq, 6eq), 2.25 (2H, \(q\), \(^3J = 7.5\), H-1\('\)), 2.13 (2H, \(dd\), \(^2J = 16.5\), \(^3J = 11.0\), H-4ax, 6ax), 2.05-1.98 (1H, \(m\), H-5), 1.38-1.24 (8H, \(m\), H-1\('\), H-2\('\), H-3\('\) and H-4\('\)), 0.94 and 0.90 (3H, \(t\), \(^3J = 6.5\), H-5\('\) and 3H, \(t\), \(^3J = 7.5\), H-2\('\)); \(^{13}\)C APT NMR (125 MHz, CD\(_3\)OD): \(\delta\) 118.2 (C, C-2), 36.6 and 33.1 (CH\(_2\), C-1\('\) and CH\(_2\), C-3\('\)), 34.8 (CH, C-5), 37.1 (CH\(_2\)), 19.6 (CH\(_3\)).
27.4 (CH₂, C-2'), 23.7 (CH₂, C-4'), 16.0 (CH₃, C-1''), 14.5 and 13.6 (CH₃, C-2'' and C-5'); m/z (EI) 210.1618 [M⁺ C₁₃H₂₂O₂ requires 210.1620 (Δ = 1.9 ppm)], 210 (36%), 183 (12), 169 (9), 153 (27), 139 (43), 125 (82), 112 (50), 111 (35), 97 (35), 84 (45), 69 (52), 55 (100), 43 (47), 41 (50).

2-ethyl-5-pentyl-1,3-cyclohexanedione “Chiloglottone 3” (1be)

Yield = 55% over two steps: IR (neat): 2955, 2930, 2870, br. 2640, 1555, 1383, 1260, 1095 cm⁻¹; ¹H NMR (500 MHz, CD₃OD): δ 2.42 (2H, d, ²J = 13.5, H-4eq, 6eq), 2.24 (2H, q, ³J = 7.0, H-1''), 2.17-2.09 (3H, m, H-4ax, 6ax and H-5), 1.33-1.24 (4H, m, H-2'' and H-3''), 1.07 (3H, d, ³J = 4.5, H-1'), 0.90 (3H, t, ³J = 7.0, H-4''); ¹³C APT NMR (125 MHz, CD₃OD): δ 116.7 (C, C-2), 32.1 (CH₂, C-2''), 29.9 (CH, C-5), 23.8 (CH₂, C-3''), 22.5 (CH₂, C-1''), 21.2 (CH₃, C-1'), 14.5 (CH₃, C-4''); m/z (EI) 182.1310 [M⁺ C₁₁H₁₈O₂ requires 182.1307 (Δ = 1.81 ppm)], 182 (4%), 165 (3), 153 (16), 140 (18), 126 (20), 111 (27), 98 (30), 84 (48), 69 (85), 55 (92), 41 (100).
5-propyl-1,3-cyclohexanedione (1da)

$^1$H NMR, 500 MHz, CD$_3$OD

$^{13}$C NMR, 125 MHz, CD$_3$OD
2-methyl-5-propyl-1,3-cyclohexanedione (1db)

$^1$H NMR, 500 MHz, CD$_3$OD
$^{13}$C NMR, 125 MHz, CD$_3$OD
2-ethyl-5-propyl-1,3-cyclohexanedione “Chiloglottone 1” (1dc)

$^1$H NMR, 500 MHz, CD$_3$OD

$^{13}$C APT NMR, 125 MHz, CD$_3$OD
2,5-dipropyl-1,3-cyclohexanedione (1dd)

$^1$H NMR, 500 MHz, CD$_3$OD
$^{13}$C NMR, 125 MHz, CD$_3$OD
2-butyl-5-propyl-1,3-cyclohexanedione (1de)

$^1$H NMR, 500 MHz, CD$_3$OD

$^{13}$C NMR, 125 MHz, CD$_3$OD
2-pentyl-5-propyl-1,3-cyclohexanedione (1df)

$^1$H NMR, 500 MHz, CD$_3$OD
$^{13}$C NMR, 125 MHz, CD$_3$OD
2-hexyl-5-propyl-1,3-cyclohexanedione (1dg)

$^1$H NMR, 500 MHz, CD$_3$OD

$^{13}$C NMR, 125 MHz, CD$_3$OD
2-ethyl-5-pentyl-1,3-cyclohexanedione “Chiloglottone 2” (1fc)

$^1$H NMR, 500 MHz, CD$_3$OD
$^{13}$C NMR, 125 MHz, CD$_3$OD
2-ethyl-5-pentyl-1,3-cyclohexanedione “Chiloglottone 3” (1be)

$^1$H NMR, 500 MHz, CD$_3$OD

$^{13}$C NMR, 125 MHz, CD$_3$OD
1,5-dimethoxy-3-ethylcyclohexa-1,4-diene (4c)

$^1$H NMR, 300 MHz, CDCl$_3$
13C APT NMR, 75 MHz, CDCl₃

1,5-dimethoxy-3-propylcyclohexa-1,4-diene (4d)
$^1$H NMR, 300 MHz, CDCl$_3$

$^{13}$C NMR, 75 MHz, CDCl$_3$
1,5-dimethoxy-3-butylcyclohexa-1,4-diene (4e)

$^1$H NMR, 300 MHz, CDCl$_3$
$^{13}$C NMR, 75 MHz, CDCl$_3$