

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

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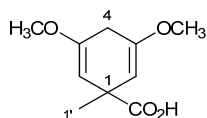
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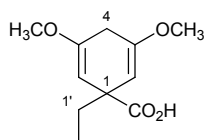
Representative Procedure for preparation of 2. Reductive alkylations were performed with adaptations to published procedures.^{1,2} To a solution of 3,5-dimethoxybenzoic acid (1 equiv.) in dry THF (2 mL/mmol) liquid NH₃ (approx. 5 mL/mmol) was condensed. Lithium (2.2 equiv.) was added in portions at -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. NH₃ was evaporated under a stream of N₂ overnight. The residue was partitioned between Et₂O and H₂O, 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 (H₂O), dried (MgSO₄) and concentrated *in vacuo*. The solid residue was recrystallized from CH₂Cl₂ to return the diene acid **2**.

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



Yield = 79% as colorless prisms. IR (neat): br. 3430, 1724, 1600 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 4.71 (2H, *dd*, ⁴*J* = 1.5, ⁴*J* = 1.5, H-2,6), 3.59 (6H, *s*, 3,5-OCH₃), 2.82 (1H, *dt*, ²*J* = 20.7, ⁴*J* = 1.5, H-4a), 2.73 (1H, *dt*, ²*J* = 20.7, ⁴*J* = 1.5, H-4b), 1.41 (3H, *s*, H-1'); ¹³C APT NMR (75 MHz, CDCl₃): δ 172.2 (C, 1-CO₂H), 152.7 (C, C-3,5), 96.4 (CH, C-2,6), 54.4 (CH₃, 3,5-OCH₃), 45.8 (C, C-1), 30.9 (CH₂, C-4), 29.0 (CH₃, C-1'); *m/z* (ESI) 199.0963 [(M+H)⁺C₁₀H₁₅O₄ requires 199.0970 (Δ = 3.6 ppm)].

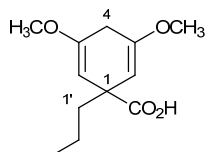
3,5-dimethoxy-1-ethylcyclohexa-2,5-dienecarboxylic acid (2c)



Yield = 78 % as colorless prisms. IR (neat): v. br. 3400, 2090, 1640 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 4.65 (2H, *dd*, ⁴*J* = 1.2, ⁴*J* = 1.2, H-2,6), 3.60 (6H, *s*, 3,5-OCH₃), 2.77-2.66 (2H, *m*, H-4), 1.75 (2H, *q*,

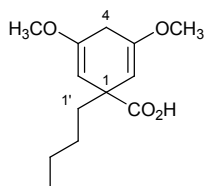
$^3J = 7.5$, H-1'), 0.82 (3H, *t*, $^3J = 7.5$, H-2'); ^{13}C APT NMR (75 MHz, CDCl_3): δ 182.5 (C, 1-CO₂H), 153.4 (C, C-3,5), 94.4 (CH, C-2,6), 54.4 (CH₃, 3,5-OCH₃), 50.3 (C, C-1), 33.7 (CH₂, C-1'), 31.1 (CH₂, C-4), 8.6 (CH₃, C-2'); *m/z* (ESI) 213.1121 [(M+H)⁺ C₁₁H₁₇O₄ requires 213.1127 ($\Delta = 2.8$ ppm)].

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



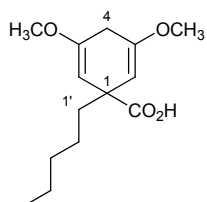
Yield = 99% as colorless prisms. IR (neat): v. br. 3400, 2090, 1643 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 4.68 (2H, *s*, H-2,6), 3.60 (6H, *s*, 3,5-OCH₃), 2.75 (2H, *s*, H-4), 1.73-1.67 (2H, *m*, H-1'), 1.31-1.20 (2H, *m*, H-2'), 0.90 (3H, *t*, $^3J = 7.2$, H-3'); ^{13}C APT NMR (75 MHz, CDCl_3): δ 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 ($\Delta = 2.8$ ppm)].

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



Yield = 77% as colorless prisms. IR (neat): v. br. 3400, 2090, 1640 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): 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'); ^{13}C APT NMR (75 MHz, CDCl_3): 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 ($\Delta = 1.2$ ppm)].

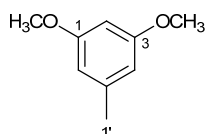
3,5-dimethoxy-1-pentylcyclohexa-2,5-dienecarboxylic acid (**2f**)



Yield = 44% as colorless prisms. IR (neat): v. br. 3400, 2090, 1643 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 4.67 (2H, *s*, H-2,6), 3.60 (6H, *s*, 3,5- OCH_3), 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'); ^{13}C APT NMR (75 MHz, CDCl_3): δ 182.8 (C, 1- CO_2H), 153.1 (C, C-3,5), 94.9 (CH, C-2,6), 54.4 (CH_3 , 3,5- OCH_3), 49.9 (C, C-1), 41.0 (CH_2 , C-1'), 32.0 (CH_2 , C-3'), 31.1 (CH_2 , C-4), 23.9 and 22.5 (CH_2 , C-2' and C-4'), 14.0 (CH_3 , C-5'); *m/z* (ESI) 255.1596 [(M+H) $^+$ $\text{C}_{14}\text{H}_{23}\text{O}_4$ requires 255.1596 ($\Delta = 0.0$ ppm)].

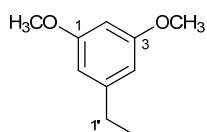
Representative Procedure for synthesis of 3: Following a published account with minor modifications;¹ to a rapidly stirred solution of **2** (1 equiv.) in benzene (20 mL/mmol) was added $\text{Pb}(\text{OAc})_4$ (1.3 equiv.). After 30-40 min, by which time the mixture had become colorless, H_2O (approx. equivolume to benzene) was added and the mixture filtered under vacuum through a plug of silica. The aqueous phase was extracted with Et_2O and the combined organic extracts washed (sat. aqueous NaHCO_3 solution), dried (MgSO_4) and the solvents removed *in vacuo* to give **3** as a pale mobile oil.

1,3-dimethoxy-5-methylbenzene (**3b**)



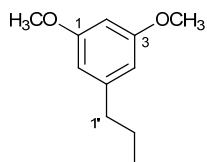
Yield = 91% as pale yellow oil: IR (neat): 2997, 2940, 2835, s. 1597, 1462, 1204, 1150, 829 cm^{-1} ; ^1H NMR: (300 MHz, CDCl_3): δ 6.35 (2H, *d*, $^4J = 2.1$, H-4,6), 6.30 (1H, *t*, $^4J = 2.1$, H-2), 3.78 (6H, *s*, 1,3- OCH_3), 2.31 (3H, *s*, H-1'); ^{13}C NMR: (75 MHz, CDCl_3): δ 160.7 (C, C-1,3), 140.2 (C, C-5), 107.0 (CH, C-4,6), 97.5 (CH, C-2), 55.2 (CH_3 , 1,3- OCH_3), 21.8 (CH_3 , C-1'); *m/z* (EI) 152.0833 [M^+ $\text{C}_9\text{H}_{12}\text{O}_2$ requires 152.0837 ($\Delta = 2.8$ ppm)].

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



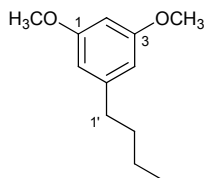
Yield = 94% as pale yellow oil: IR (neat): 2997, 2943, 2835, s. 1598, 1462, 1204, 1145, 829 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 6.37 (2H, *d*, $^4J = 2.1$, H-4,6), 6.30 (1H, *t*, $^4J = 2.1$, H-2), 3.79 (6H, *s*, 1,3- OCH_3), 2.60 (2H, *q*, $^3J = 7.5$, H-1'), 1.23 (3H, *t*, $^3J = 7.5$, H-2'); ^{13}C APT NMR (75 MHz, CDCl_3): 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 (CH_3 , 1,3- OCH_3), 29.2 (CH_2 , C-1'), 15.4 (CH_3 , C-2'); *m/z* (EI) 166.0992 [M^+ $\text{C}_{10}\text{H}_{14}\text{O}_2$ requires 166.0994 ($\Delta = 1.1$ ppm)].

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



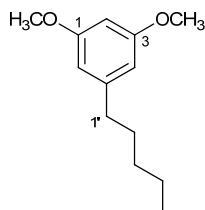
Yield = 99% as a pale yellow oil: IR (neat): 2997, 2959, 2832, s. 1597, 1462, 1204, 1150, 829 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 6.35 (2H, *d*, $^4J = 2.1$, H-4,6), 6.30 (1H, *t*, $^4J = 2.1$, H-2), 3.78 (6H, *s*, 1,3- OCH_3), 2.53 (2H, *t*, $^3J = 7.5$, H-1'), 1.63 (2H, *tq*, $^3J = 7.5$, $^3J = 7.5$, H-2'), 1.23 (3H, *t*, $^3J = 7.5$, H-3'); ^{13}C NMR APT NMR (75 MHz, CDCl_3): 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 (CH_3 , 1,3- OCH_3), 38.4 (CH_2 , C-1'), 24.3 (CH_2 , C-2'), 13.9 (CH_3 , C-3'); *m/z* (EI) 180.1149 [M^+ $\text{C}_{11}\text{H}_{16}\text{O}_2$ requires 180.1150 ($\Delta = 0.7$ 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, CDCl_3): 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- OCH_3), 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'); ^{13}C NMR APT NMR (75 MHz, CDCl_3): 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 (CH_3 , 1,3- OCH_3), 36.0 (CH_2 , C-1'), 33.4 (CH_2 , C-2'), 22.4 (CH_2 , C-3'), 13.9 (CH_3 , C-4'); *m/z* (EI) 194.1307 [$\text{M}^{+\bullet}$ $\text{C}_{12}\text{H}_{18}\text{O}_2$ requires 194.1307 ($\Delta = 0.1$ ppm)].

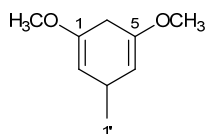
1,3-dimethoxy-5-pentylbenzene (3f)



Yield = 84% as a clear colourless oil: IR (neat): 2997, 2959, 2835, s. 1602, 1462, 1198, 1149, 829 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): 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- OCH_3), 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'); ^{13}C NMR APT NMR (75 MHz, CDCl_3): 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- OCH_3), 36.3 (CH_2 , C-1'), 31.5 and 30.9 (CH_2 , C-2' and C-3'), 22.5 (CH_2 , C-4'), 14.0 (CH_3 , C-5'); *m/z* (EI) 208.1460 [$\text{M}^{+\bullet}$ $\text{C}_{13}\text{H}_{20}\text{O}_2$ requires 208.1463 ($\Delta = 1.7$ ppm)].

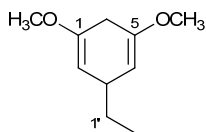
Representative Procedure for preparation of 4: To a solution of **3** (1 equiv.) in dry THF (approx. 4.5 mL/mmol) and *t*BuOH (approx. 4.5 mL/mmol), NH₃ (approx. 10-15 mL/mmol) was condensed. Lithium (17 equiv.) was added in portions at -33°C and the solution allowed to warm slowly to r.t. NH₃ was evaporated 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**)



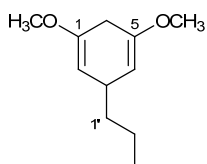
Yield = 61% as a pale yellow oil. IR (neat): 3000, 2955, 2865, s. 1600, 1382, 1205, 1150, 825 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 4.57 (2H, *ddd*, ³*J* = 3.3, ⁴*J* = 1.2, ⁴*J* = 1.2, H-2,4), 3.56 (6H, *s*, 1,5-OCH₃), 3.04 (1H, *qtdd*, ³*J* = 6.9, ³*J* = 3.3, ⁵*J* = 6.9, ⁵*J* = 6.9, H-3), 2.81-2.71 (2H, *m*, H-6), 1.08 (3H, *d*, ³*J* = 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**)



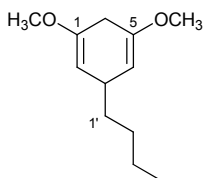
Yield = 83% as a clear colourless oil. b.p. 145°C @ 1.5mmHg; IR (neat): 3059, 2997, 2959, 2824, s. 1694, 1663, 1597, 1443, 1397, 1234, 1207, 1150 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 4.58-4.57 (2H, *m*, H-2,4), 3.57 (6H, *s*, 1,5-OCH₃), 2.94 (1H, *tddd*, ³*J* = 7.0, ³*J* = 3.3, ⁵*J* = 6.6, ⁵*J* = 6.6, H-3), 2.77-2.76 (2H, *m* [apparent *d*], *J* = 6.5, H-6), 1.43 (2H, *dq*, ³*J* = 7.0, ³*J* = 7.0, H-1'), 0.87 (3H, *t*, ³*J* = 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*, ³*J* = 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)].

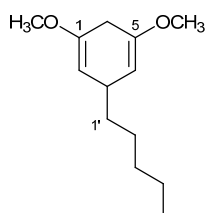
1,5-dimethoxy-3-butylcyclohexa-1,4-diene (4e)



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*, ³*J* = 3.3,

$^4J = 1.2$, $^4J = 1.2$, H-2,4), 3.56 (6H, *s*, 1,5-OCH₃), 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'); ¹³C APT NMR (75 MHz, CDCl₃): δ 151.6 (C, C-1,5), 96.1 (CH, C-2,4), 54.1 (CH₃, 1,5-OCH₃), 38.1 (CH₂, C-1'), 35.6 (CH, C-3), 31.3 (CH₂, C-6), 28.5 (CH₂, C-2'), 23.0 (CH₂, C-3'), 14.1 (CH₃, C-4'); *m/z* (EI) 196.1463 [M⁺ C₁₂H₂₀O₂ requires 196.1460 (Δ = 1.9 ppm)].

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



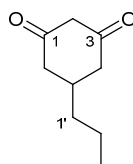
Yield = 85% as a pale yellow oil; IR (neat): 3059, 2997, 2955, 2928, 2870, *s*. 1695, 1663, 1610, 1443, 1204, 1150 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 4.59 (2H, *d*, $^3J = 3.6$, H-2,4), 3.56 (6H, *s*, 1,5-OCH₃), 2.96 (1H, *ttdd*, $^3J = 7.2$, $^3J = 3.6$, $^5J = 7.2$, $^5J = 7.2$, H-3), 2.78-2.75 (2H, *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'); ¹³C APT NMR (75 MHz, CDCl₃): δ 151.6 (C, C-1,5), 96.1 (CH, C-2,4), 54.1 (CH₃, 1,5-OCH₃), 38.3 (CH₂, C-1'), 35.6 (CH, C-3), 31.3 (CH₂, C-6), 32.2 and 26.0 (CH₂, C-2' and C-3'), 22.7 (CH₂, C-4'), 14.1 (CH₃, C-5'); *m/z* (ESI) 211.1696 [(M+H)⁺ C₁₃H₂₃O₂ requires 211.1698 (Δ = 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/mmol) was cooled to -78°C. *t*BuLi (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 H₂O. The aqueous residue was

extracted with Et₂O, the combined organic phases dried (MgSO₄) and the solvents removed *in vacuo*, returning **5**, which was immediately hydrolyzed to **1**, without separation of diastereomers.

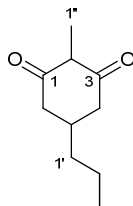
Representative Procedure for synthesis of 1: With modifications on a reported method,⁴ crude **5** (1 equiv.) was dissolved in acetone (5 mL/mmol) and aq. 2N HCl (3 equiv.) added. The resulting solution was stirred overnight at r.t. The acetone was evaporated under reduced pressure and the residue diluted (H₂O), basified (aq. 1N NaOH) and washed with Et₂O. The aqueous layer was reacidified (pH 1-3 aq. 2N HCl) and extracted with EtOAc. The organic phase was dried (MgSO₄) and concentrated *in vacuo* to return **1** as a white solid.

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



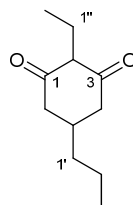
Yield = 88% as spreading colorless crystals: m.p. 95-99°C; IR (neat): br. 3310, 2957, 2930, 2872, br. 2550, 1572, 1232 cm⁻¹; ¹H NMR (500 MHz, CD₃OD): δ 2.40 (2H, *d*, ²*J* = 12.5, H-4_{eq}, 6_{eq}), 2.12-2.09 (1H, *m*, H-5), 2.10 (2H, *d*, ²*J* = 12.5, H-4_{ax}, 6_{ax}), 1.39-1.38 (4H, *m*, H-1' and H-2'), 0.93 (3H, *t*, ³*J* = 7.0, H-3'); ¹³C APT NMR (125 MHz, CD₃OD): δ 104.3 (CH, C-2), 39.7 (br, CH₂, C-4,6), 38.8 (CH₂, C-1'), 34.9 (CH, C-5), 20.8 (CH₂, C-2'), 14.4 (CH₃, C-3'); *m/z* (EI) 154.0992 [*M*⁺ C₉H₁₄O₂ requires 154.0994 (Δ = 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)



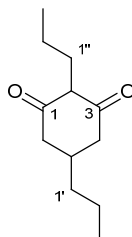
Yield = 92% over two steps. m.p. 111-115°C; IR (neat): br. 3060, 2955, 2930, 2872, br. 2650, 1572, 1383, 1242, 1088 cm^{-1} ; ^1H NMR (500 MHz, CD_3OD): δ 2.44 (2H, *dd*, $^2J = 16.5$, $^3J = 4.0$, H-4eq, 6eq), 2.13 (2H, *dd*, $^2J = 16.5$, $^3J = 11.0$, H-4ax, 6ax), 2.06-2.01 (1H, *m*, H₅), 1.63 (3H, *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_3OD): δ 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^+ $\text{C}_{10}\text{H}_{16}\text{O}_2$ 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)



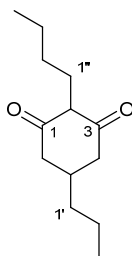
Yield = 82% over two steps. m.p. 124-126°C; IR (neat): 2957, 2928, 2872, br. 2640, 1557, 1383, 1263, 1244, 1105 cm^{-1} ; ^1H NMR (500 MHz, CD_3OD): δ 2.46 (2H, *dd*, $^2J = 16.5$, $^3J = 4.3$, H-4eq, 6eq), 2.25 (2H, *q*, $^3J = 7.5$, H-1''), 2.14 (2H, *dd*, $^2J = 16.5$, $^3J = 11.3$, H-4ax, 6ax), 2.07-2.01 (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_3OD): δ 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^+ $\text{C}_{11}\text{H}_{18}\text{O}_2$ 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**)



Yield = 75% over two steps. m.p. 133-138°C; IR (neat): br. 3425, 2957, 2928, 2872, br. 2640, 1566, 1383, 1240, 1233, 1113 cm^{-1} ; ^1H NMR (500 MHz, CD_3OD): δ 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, *m*, 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''); ^{13}C APT NMR (125 MHz, CD_3OD): δ 116.6 (C, C-2), 38.9 (CH_2 , C-1'), 34.5 (CH, C-5), 24.7 (CH_2 , C-1''), 22.8 (CH_2 , C-2''), 20.8 (CH_2 , C-2'), 14.43 and 14.38 (CH_3 , C-3' and C-3''); *m/z* (EI) 196.1457 [$\text{M}^{+\bullet}$ $\text{C}_{12}\text{H}_{20}\text{O}_2$ requires 196.1463 ($\Delta = 3.3$ ppm)], 196 (33%), 181 (32), 167 (32), 154 (14), 139 (29), 125 (30), 111 (67), 97 (100), 84 (40), 69 (22), 55 (82).

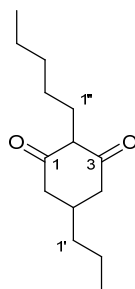
2-butyl-5-propyl-1,3-cyclohexanedione (**1de**)



Yield = 81% over two steps. m.p. 141-146 °C; IR (neat): br. 3050, 2957, 2926, 2872, br. 2621, 1568, 1383, 1242, 1115 cm^{-1} ; ^1H NMR (500 MHz, CD_3OD): δ 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''); ^{13}C APT NMR (125 MHz, CD_3OD): δ 116.8 (C, C-2), 40.5 (br, CH_2 , C-4,6),

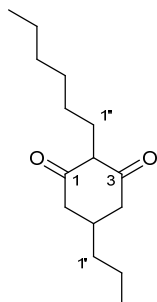
38.9 (CH₂, C-1'), 34.5 (CH, C-5), 32.0 (CH₂, C-2''), 23.8 (CH₂, C-3''), 22.4 (CH₂, C-1''), 20.8 (CH₂, C-2'), 14.5 and 14.4 (CH₃, C-3' and C-4''); *m/z* (EI) 210.1618 [$M^{+\bullet}$ C₁₃H₂₂O₂ requires 210.1620 (Δ = 0.6 ppm)], 210 (19%), 195 (6), 181 (38), 167 (34), 155 (28), 139 (27), 125 (37), 111 (56), 97 (100), 84 (37), 69 (25), 55 (67).

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



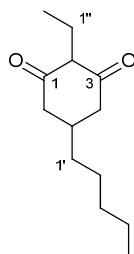
Yield = 69% over two steps. m.p. 139-143°C; IR (neat): br. 3450, 2957, 2928, 2872, br. 2633, 1568, 1385, 1242, 1115 cm⁻¹; ¹H NMR (500 MHz, CD₃OD): δ 2.44 (2H, *dd*, ²*J* = 16.5, ³*J* = 3.5, H-4_{eq}, 6_{eq}), 2.20 (2H, *t*, ³*J* = 7.0, H-1''), 2.13 (2H, *dd*, ²*J* = 16.5, ³*J* = 11.0, H-4_{ax}, 6_{ax}), 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*, ³*J* = 7.0, H-3'), 0.87 (3H, *t*, ³*J* = 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 [$M^{+\bullet}$ 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} ; ^1H NMR (500 MHz, CD_3OD): δ 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_3OD): δ 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 [$\text{M}^{+\bullet}$ $\text{C}_{15}\text{H}_{26}\text{O}_2$ requires 238.1933 ($\Delta = 1.2$ 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).

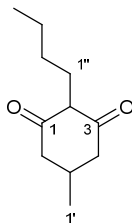
2-ethyl-5-pentyl-1,3-cyclohexanedione "Chiloglottone 2" (1fc)



Yield = 72% over two steps. IR (neat): br. 3448, 2957, 2928, 2872, br. 2639, 1560, 1385, 1242, 1108 cm^{-1} ; ^1H NMR (500 MHz, CD_3OD): δ 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_3OD): δ 118.2 (C, C-2), 36.6 and 33.1 (CH_2 , C-1' and CH_2 , C-3'), 34.8 (CH, C-5),

27.4 (CH₂, C-2'), 23.7 (CH₂, C-4'), 16.0 (CH₂, C-1''), 14.5 and 13.6 (CH₃, C-2'' and C-5'); *m/z* (EI) 210.1618 [M^{+} C₁₃H₂₂O₂ requires 210.1620 ($\Delta = 1.9$ 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).

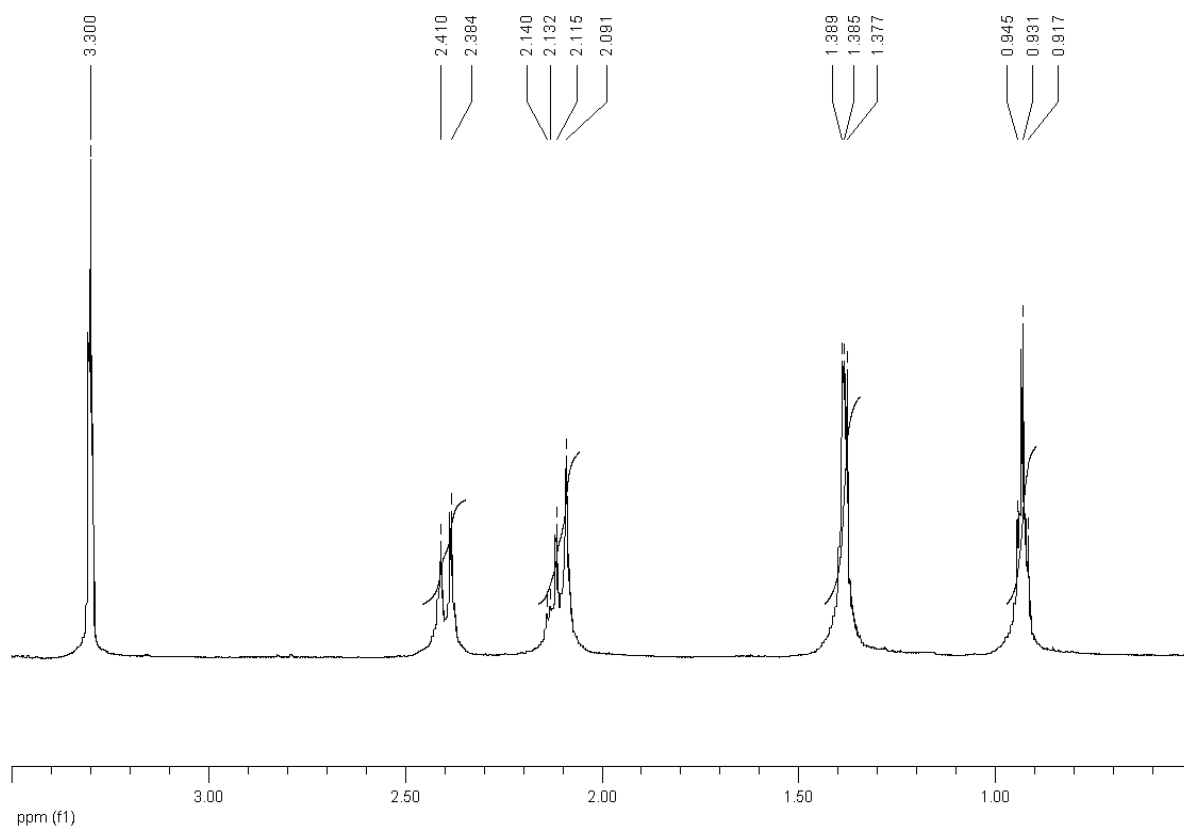
2-ethyl-5-pentyl-1,3-cyclohexanedione “Chiloglottone 3” (1be)



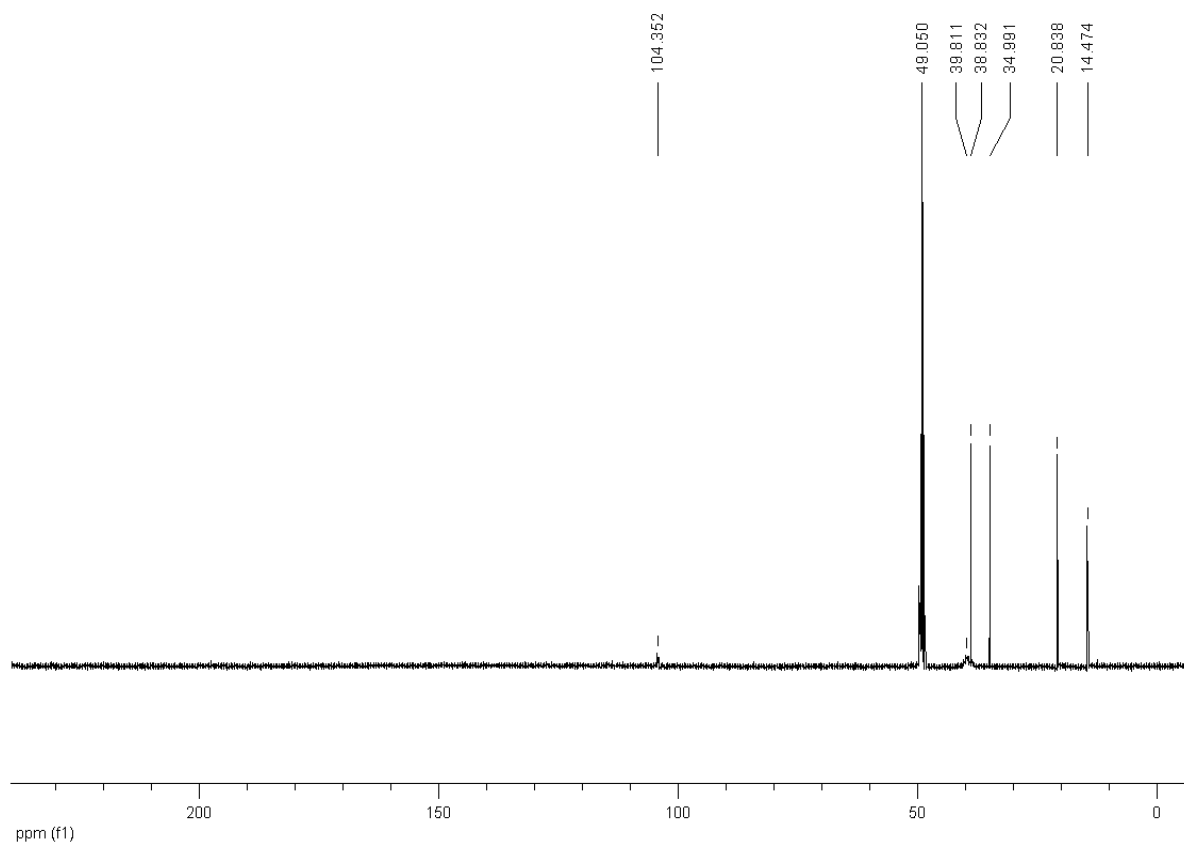
Yield = 55% over two steps: IR (neat): 2955, 2930, 2870, br. 2640, 1555, 1383, 1260, 1095 cm⁻¹; ¹H NMR (500 MHz, CD₃OD): δ 2.42 (2H, *d*, ²*J* = 13.5, H-4eq, 6eq), 2.24 (2H, *q*, ³*J* = 7.0, H-1''), 2.17-2.09 (3H, *m*, H-4ax, 6ax and H-5), 1.33-1.24 (4H, *m*, H-2'' and H-3''), 1.07 (3H, *d*, ³*J* = 4.5, H-1'), 0.90 (3H, *t*, ³*J* = 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 ($\Delta = 1.81$ 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)

^1H NMR, 500 MHz, CD_3OD

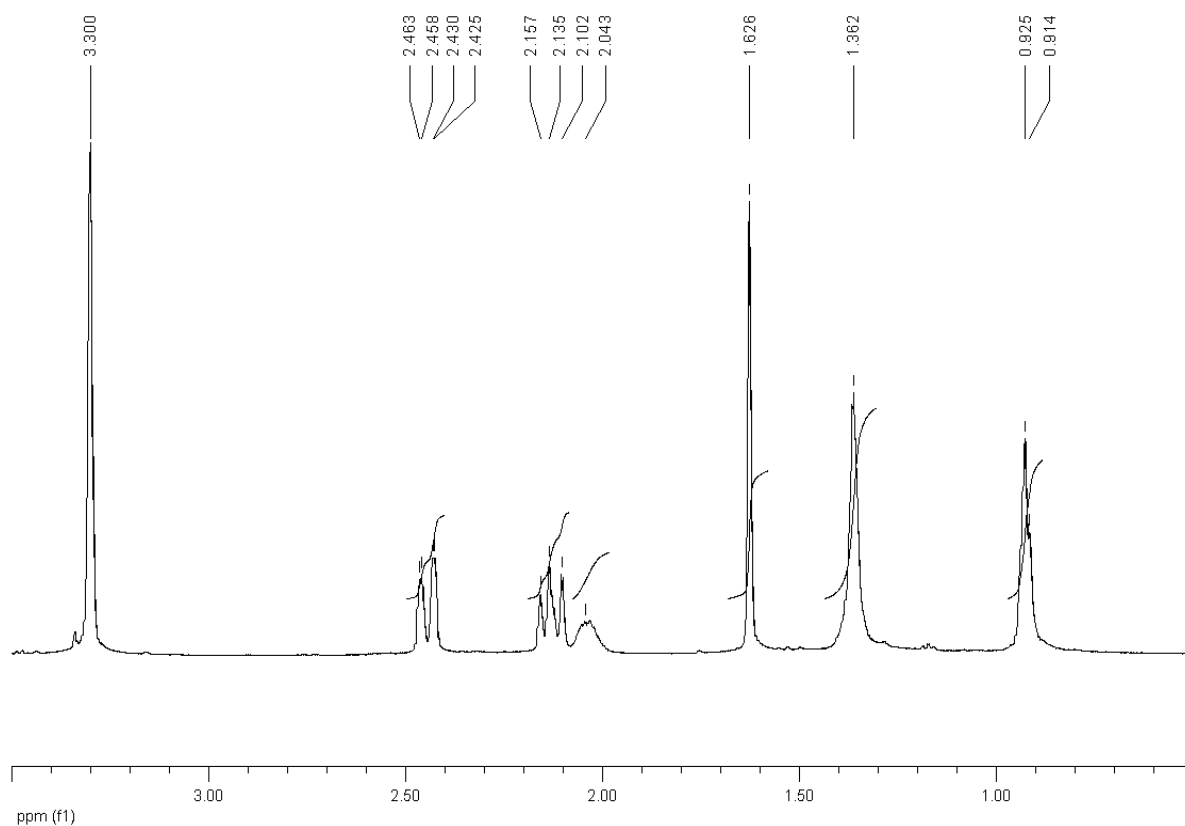


^{13}C NMR, 125 MHz, CD_3OD

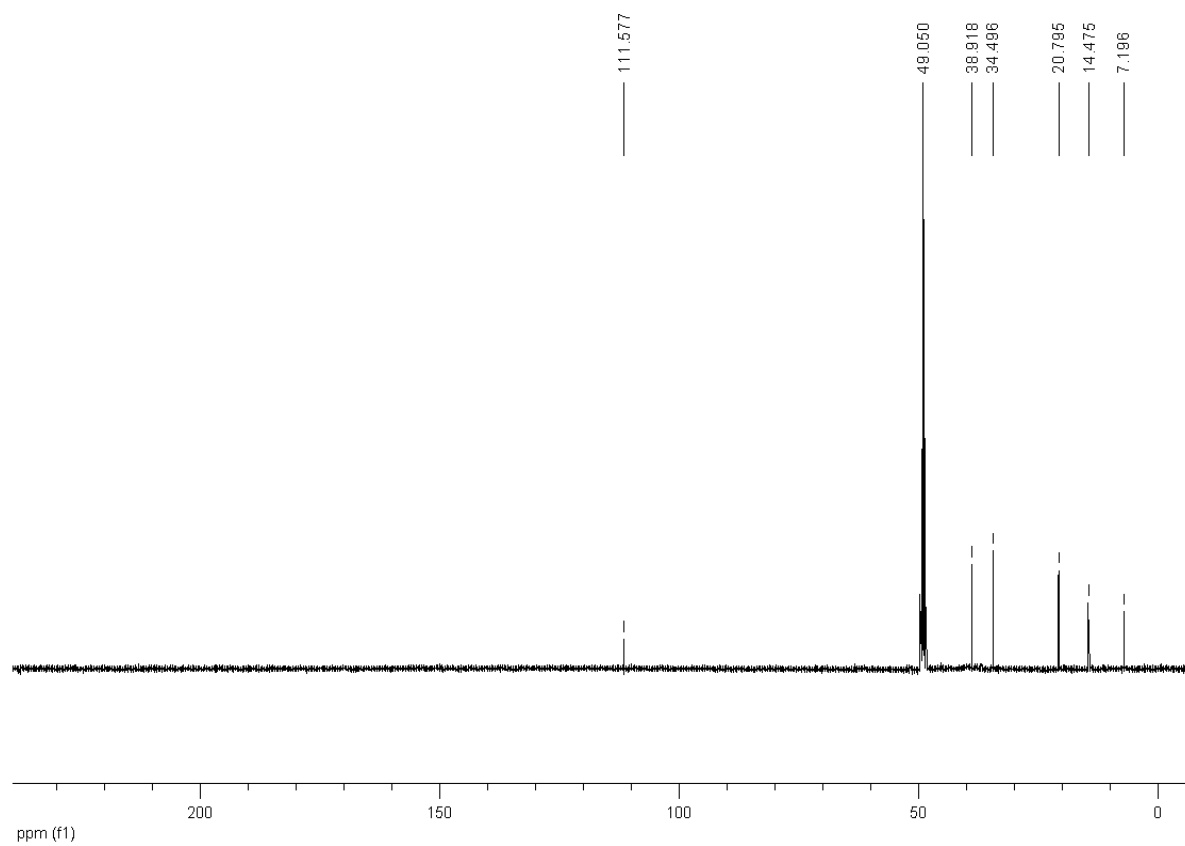


2-methyl-5-propyl-1,3-cyclohexanedione (1db)

¹H NMR, 500 MHz, CD₃OD

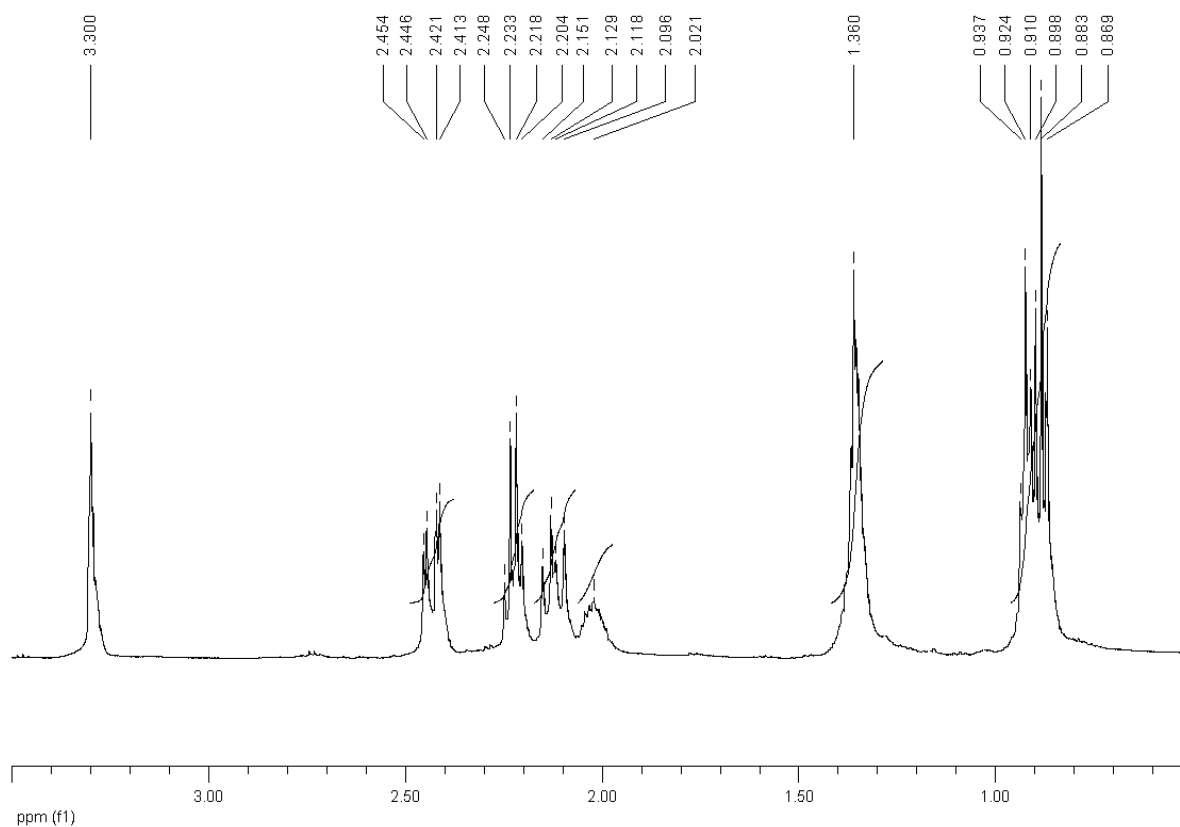


^{13}C NMR, 125 MHz, CD_3OD

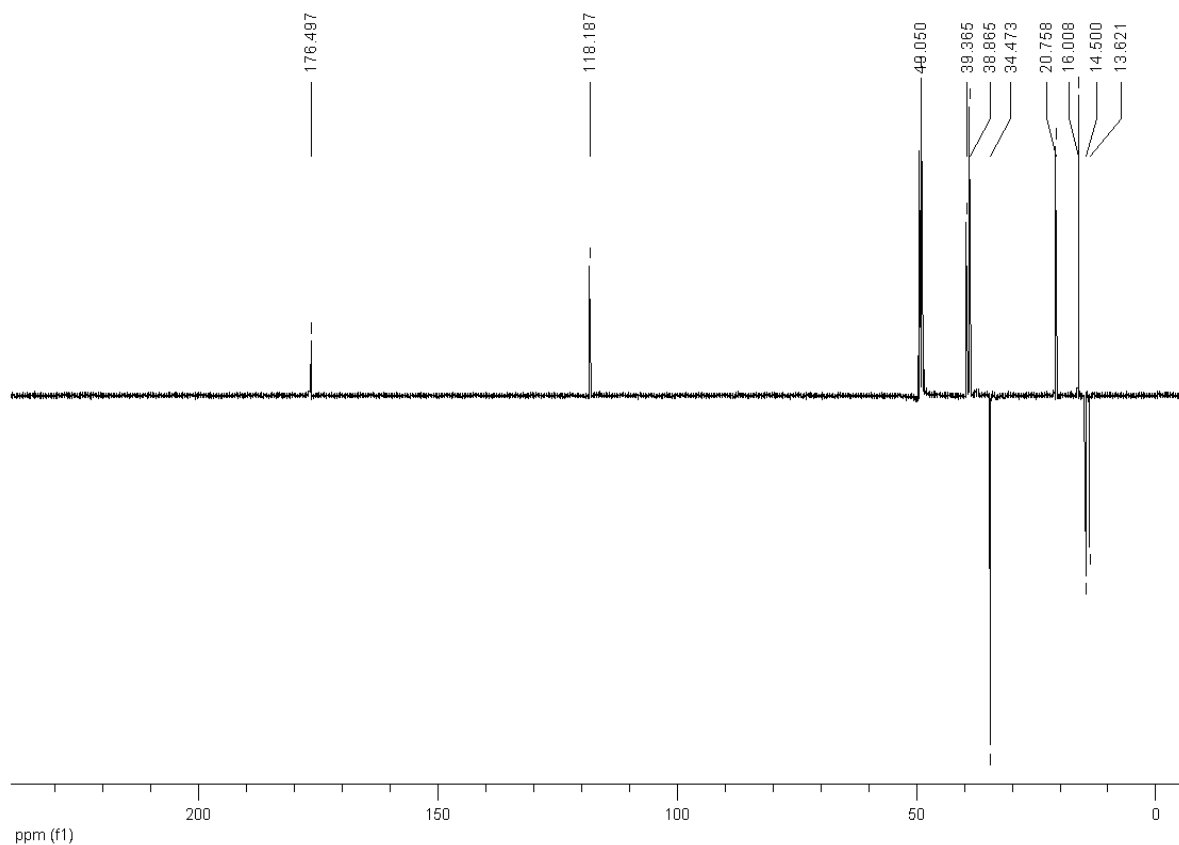


2-ethyl-5-propyl-1,3-cyclohexanedione "Chiloglottone 1" (1dc)

^1H NMR, 500 MHz, CD_3OD

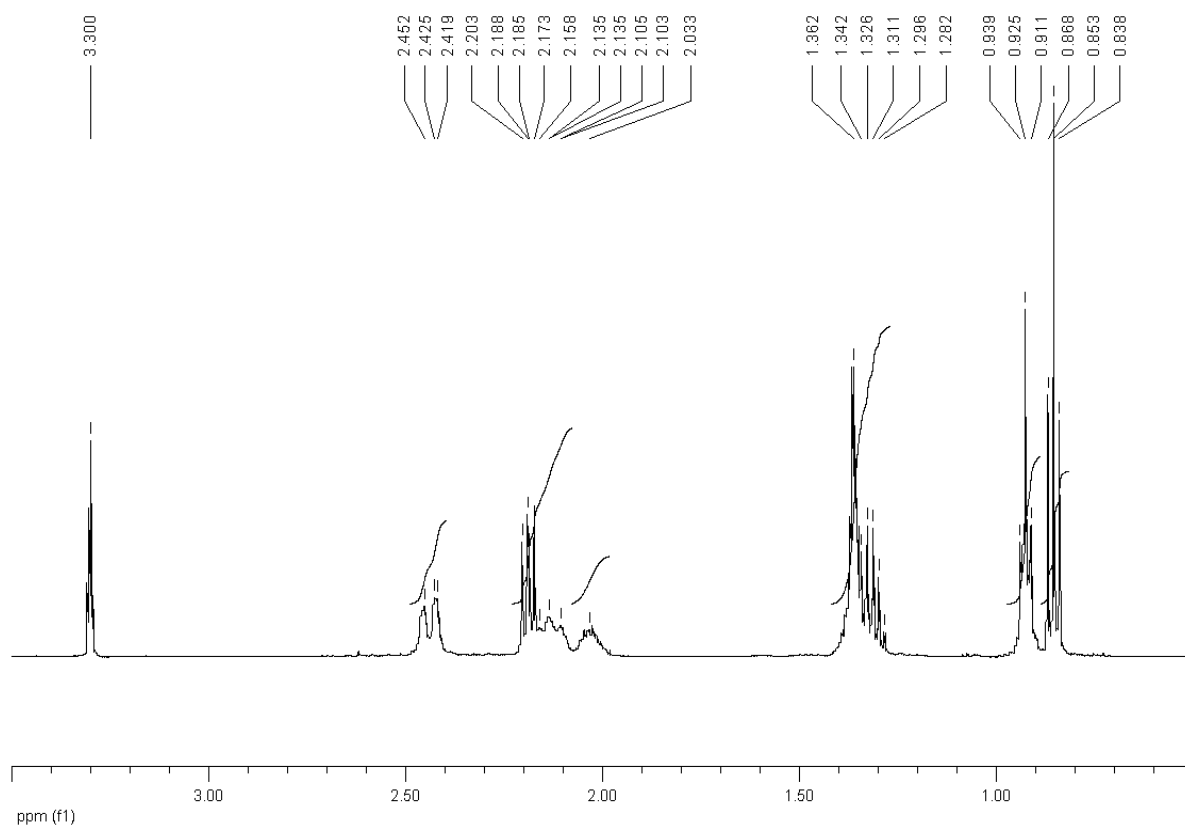


^{13}C APT NMR, 125 MHz, CD_3OD

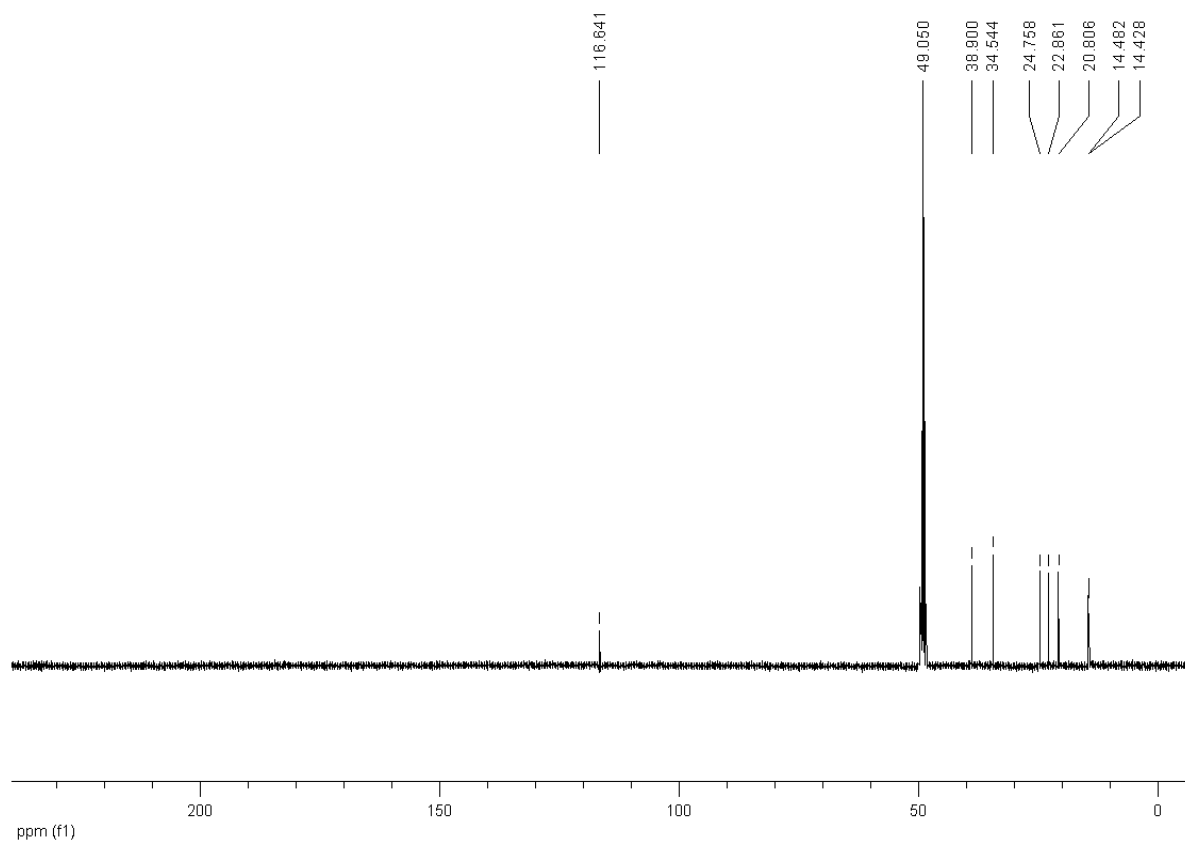


2,5-dipropyl-1,3-cyclohexanedione (1dd)

¹H NMR, 500 MHz, CD₃OD

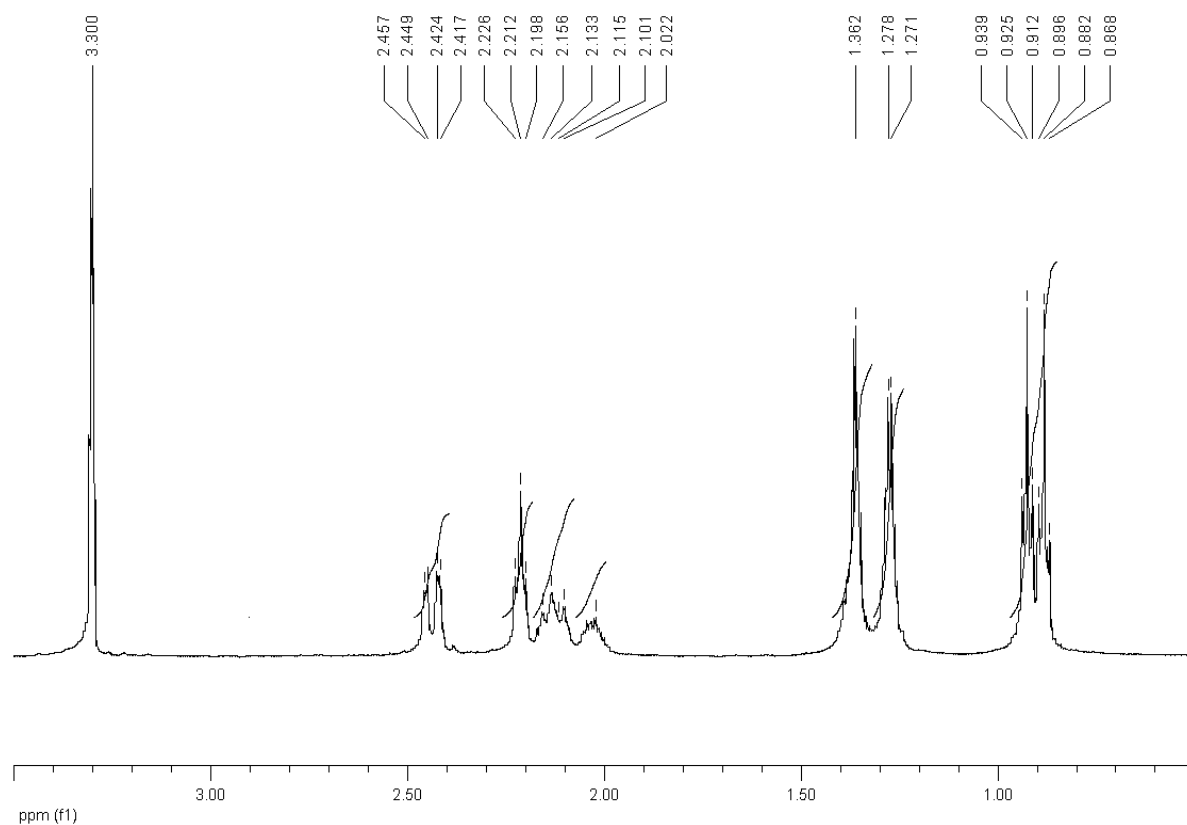


^{13}C NMR, 125 MHz, CD_3OD

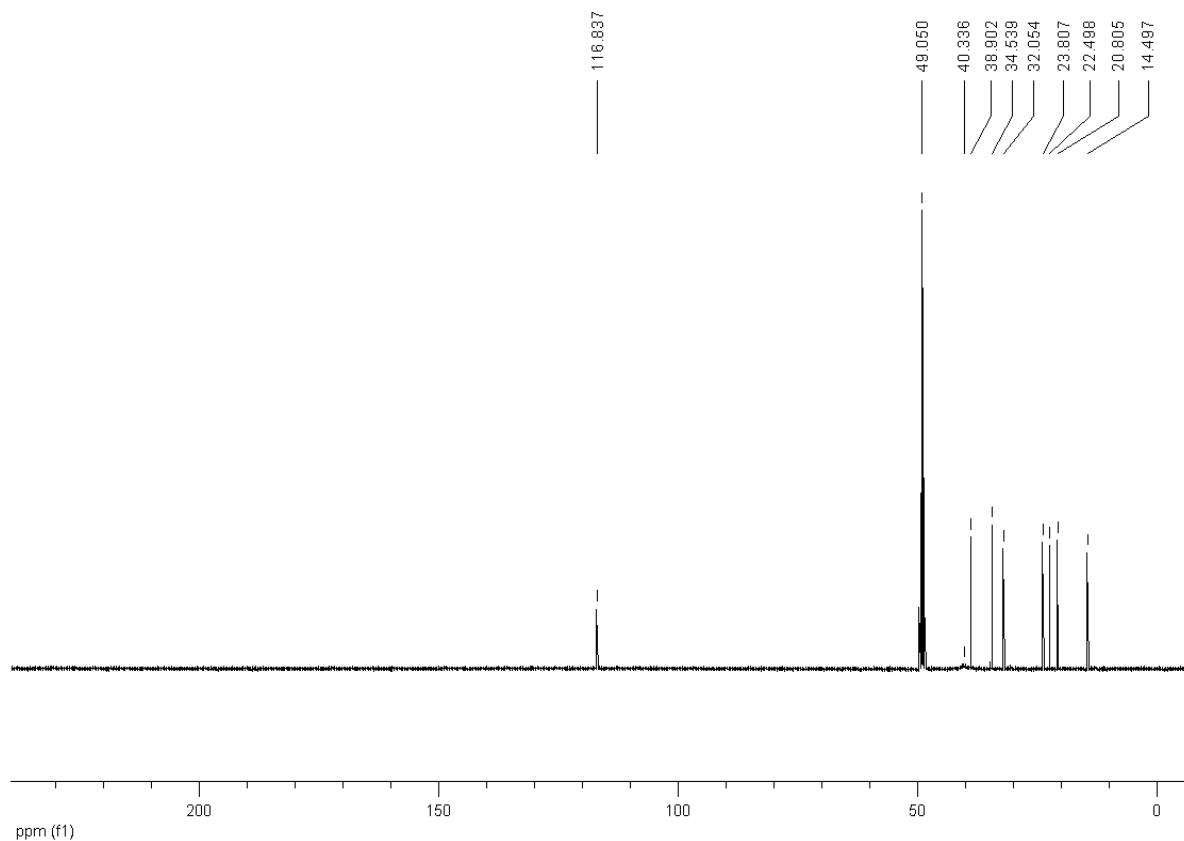


2-butyl-5-propyl-1,3-cyclohexanedione (1de)

^1H NMR, 500 MHz, CD_3OD

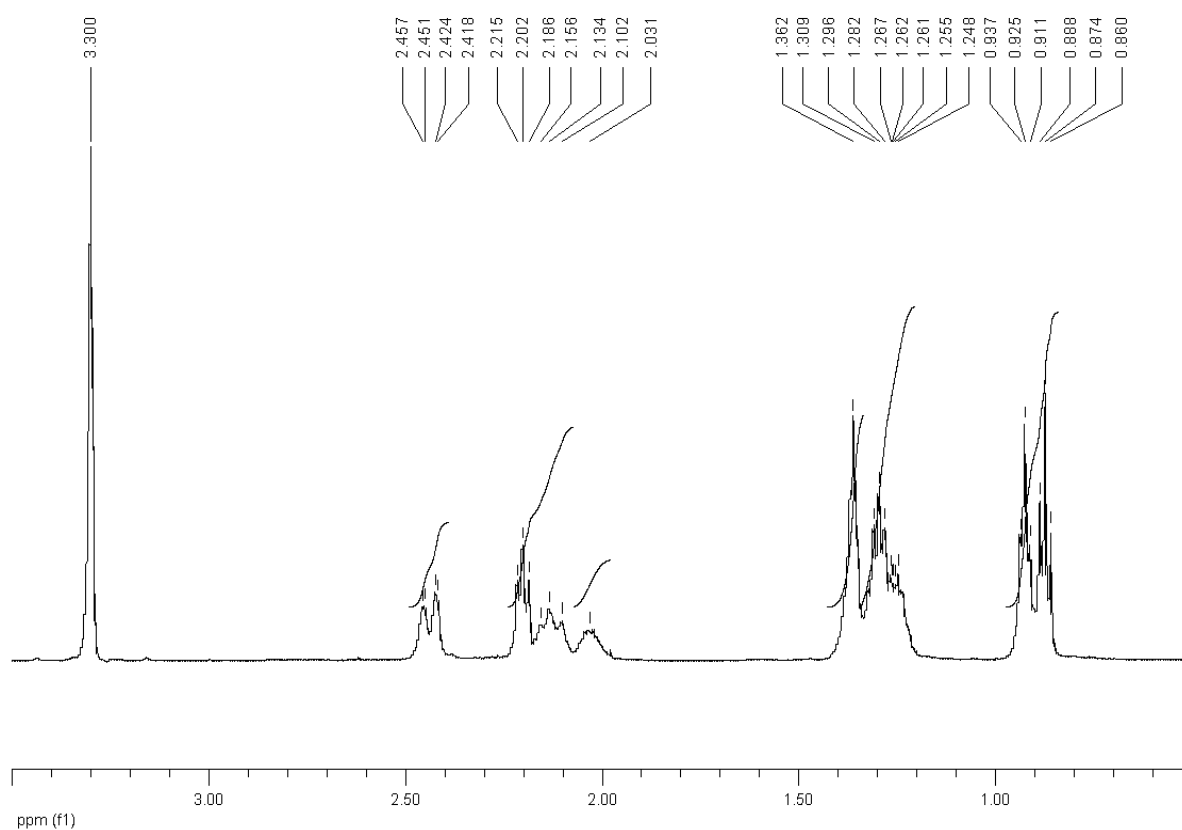


^{13}C NMR, 125 MHz, CD_3OD

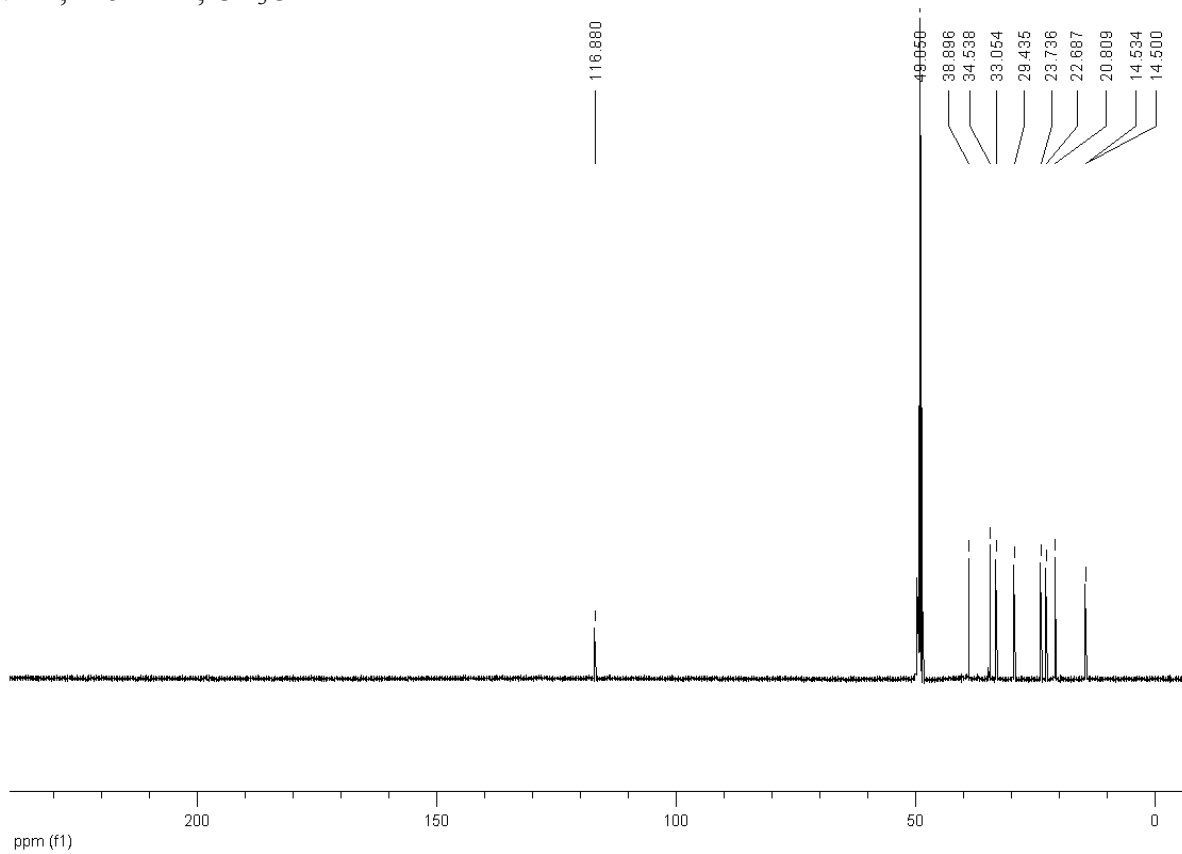


2-pentyl-5-propyl-1,3-cyclohexanedione (1df)

¹H NMR, 500 MHz, CD₃OD

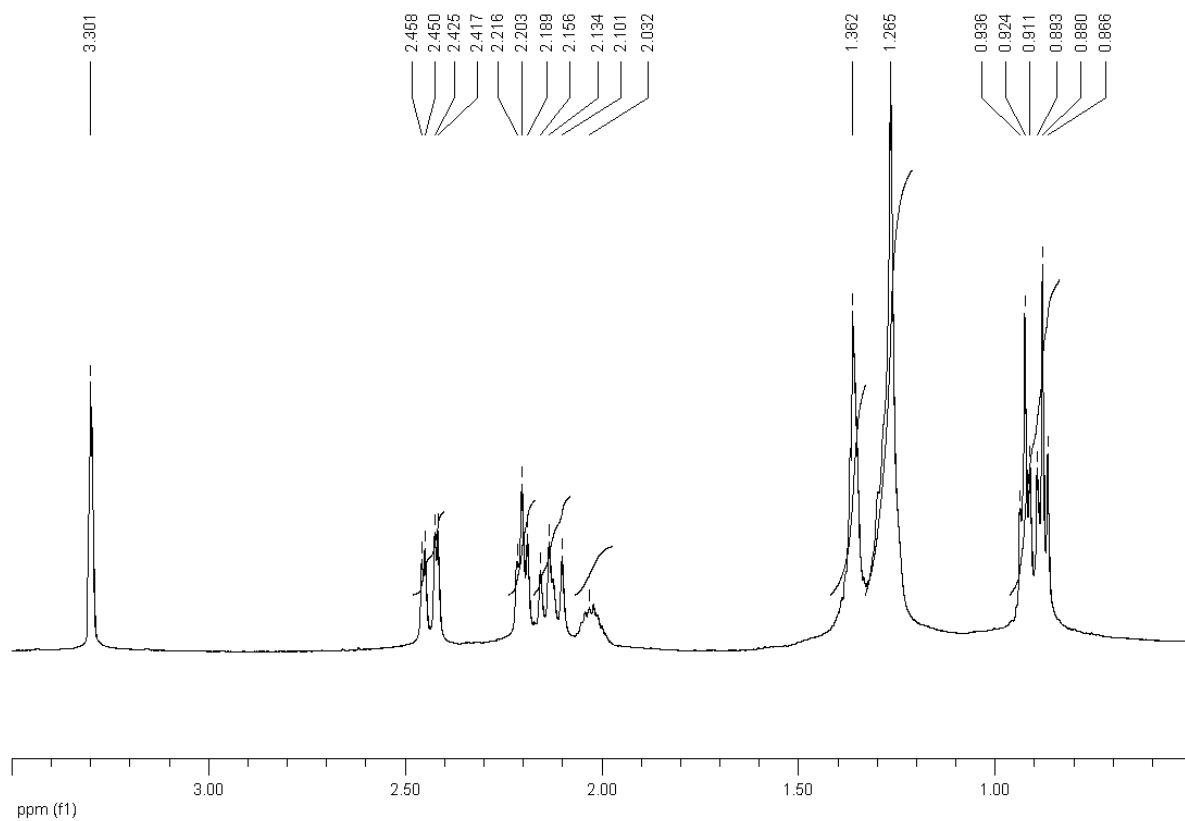


¹³C NMR, 125 MHz, CD₃OD

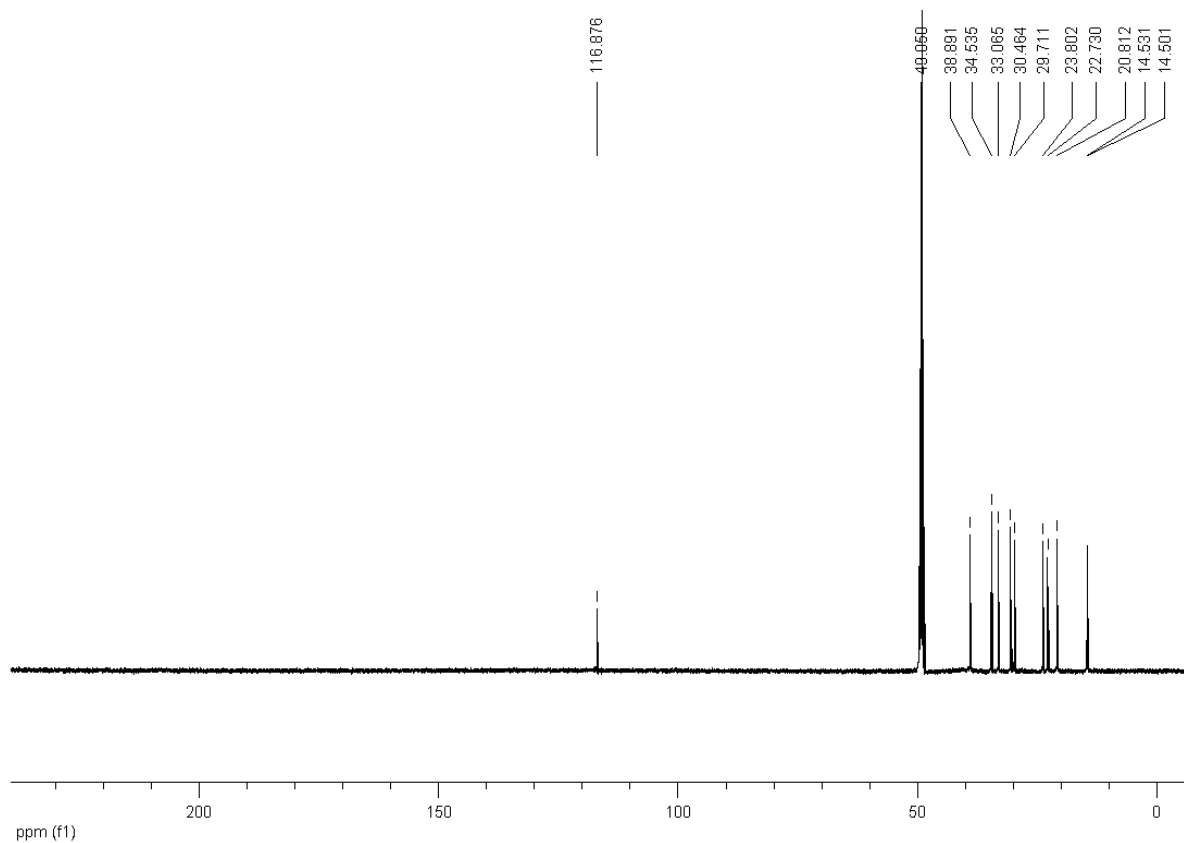


2-hexyl-5-propyl-1,3-cyclohexanedione (1dg)

^1H NMR, 500 MHz, CD_3OD

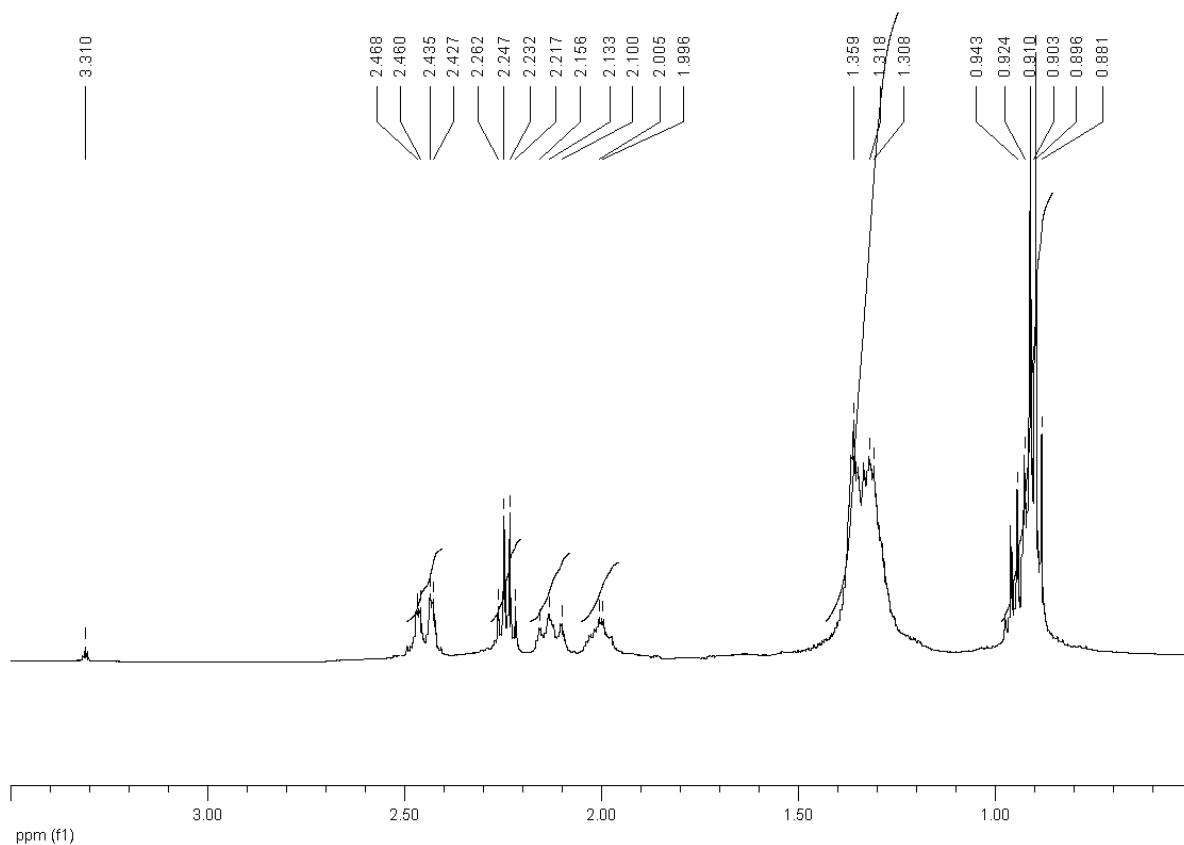


^{13}C NMR, 125 MHz, CD_3OD

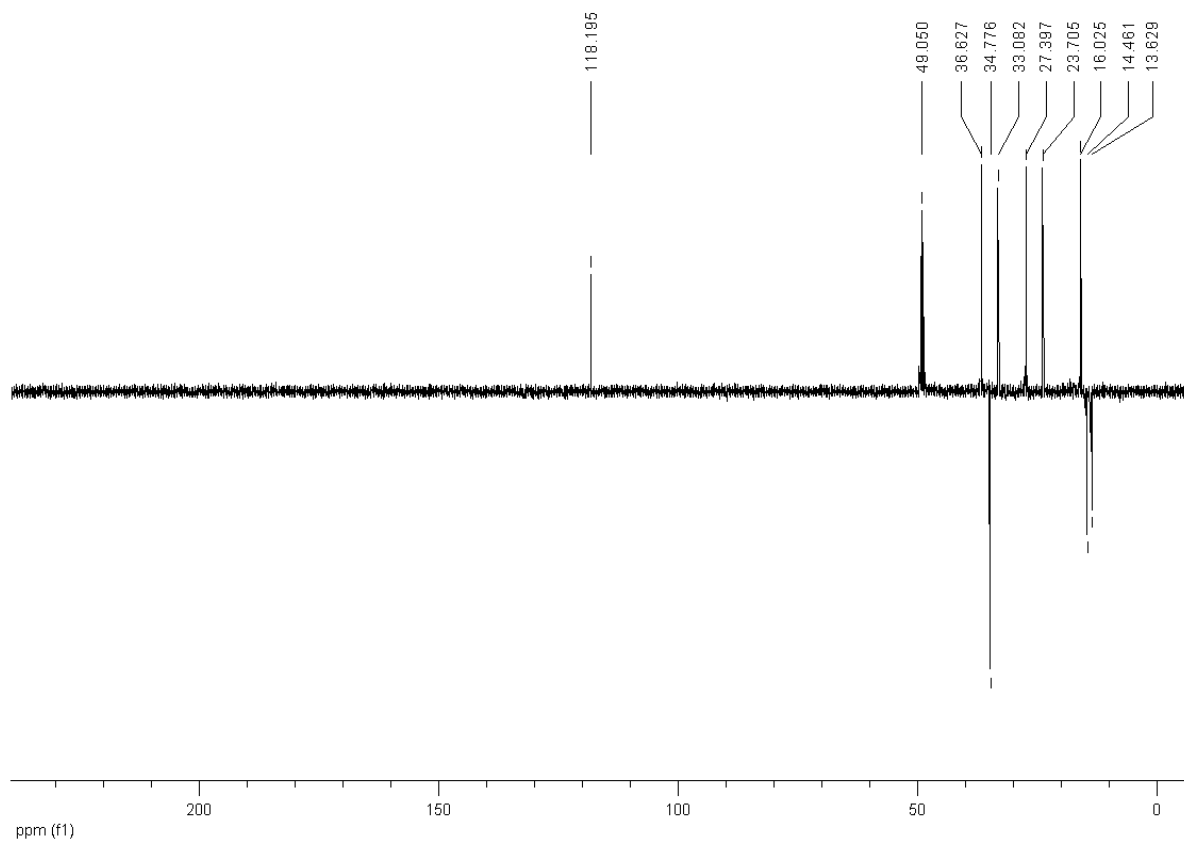


2-ethyl-5-pentyl-1,3-cyclohexanedione "Chiloglottone 2" (1c)

¹H NMR, 500 MHz, CD₃OD

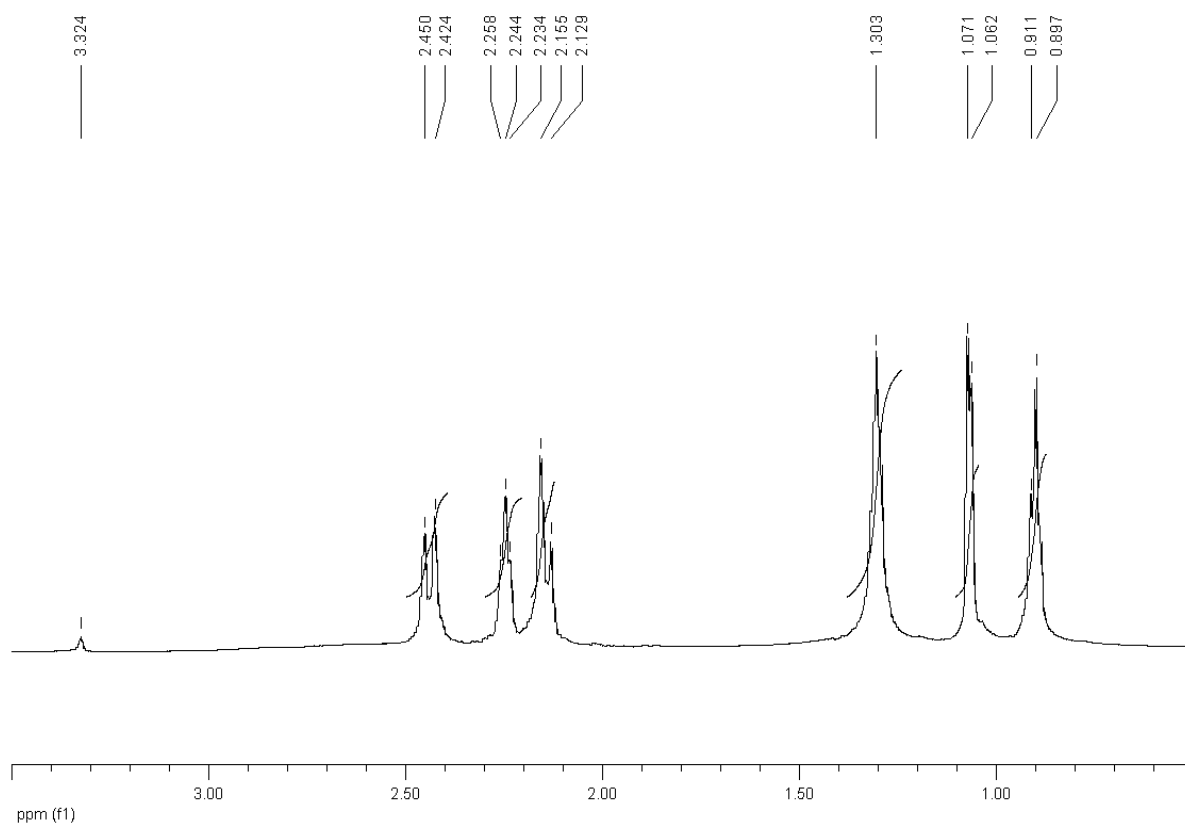


^{13}C NMR, 125 MHz, CD_3OD

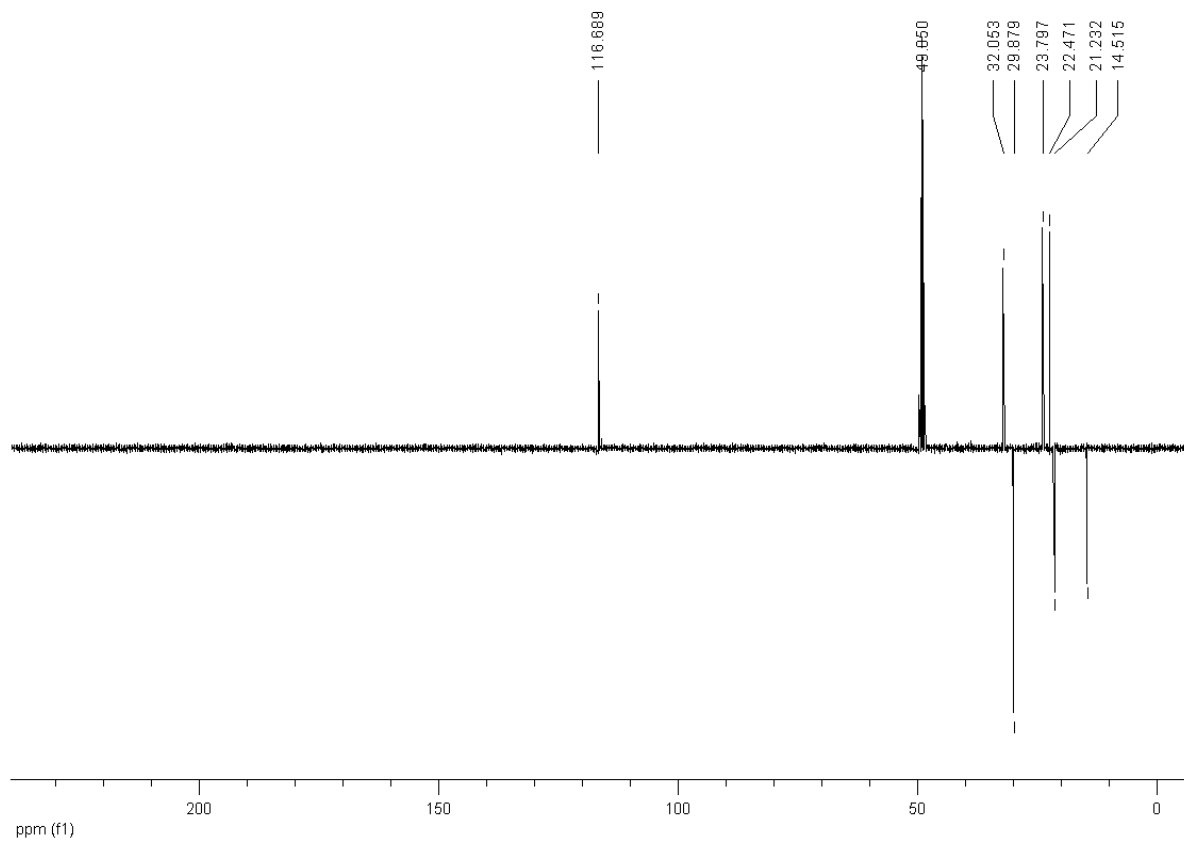


2-ethyl-5-pentyl-1,3-cyclohexanedione “Chiloglottone 3” (1be)

^1H NMR, 500 MHz, CD_3OD

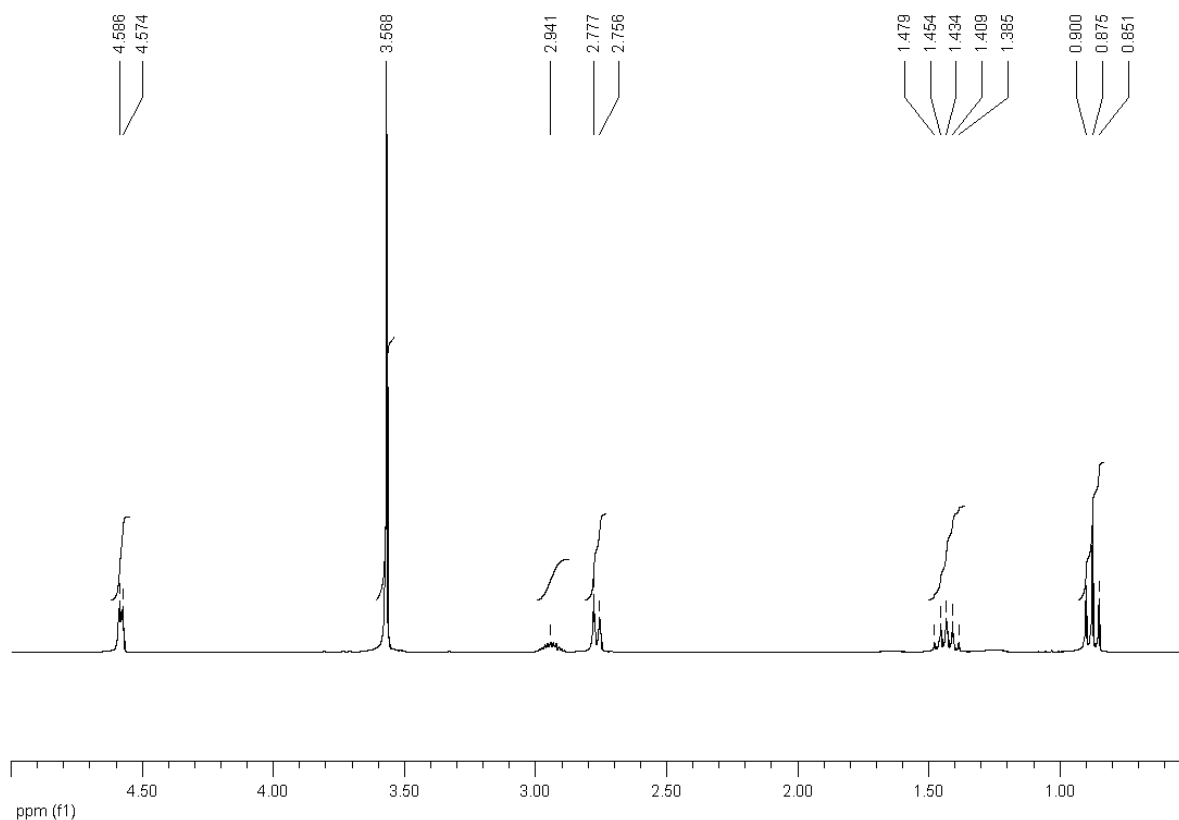


^{13}C NMR, 125 MHz, CD_3OD

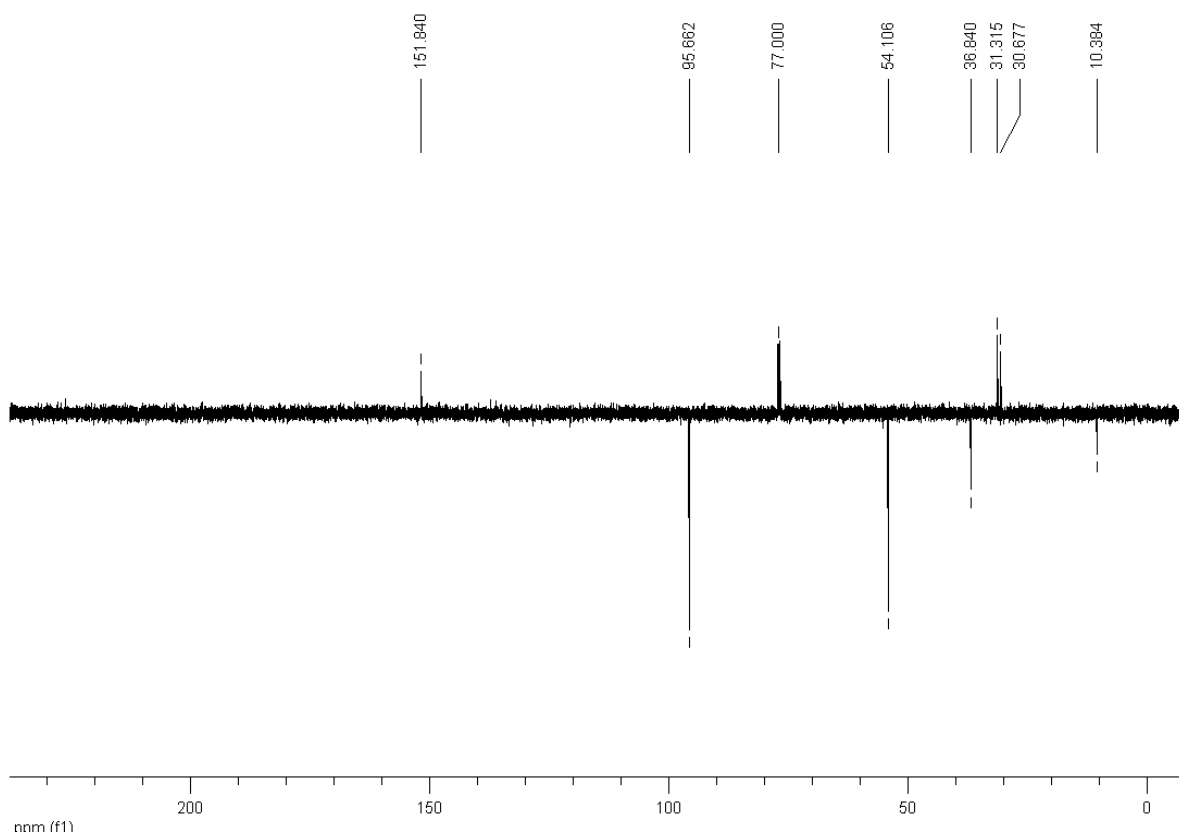


1,5-dimethoxy-3-ethylcyclohexa-1,4-diene (4c)

¹H NMR, 300 MHz, CDCl₃

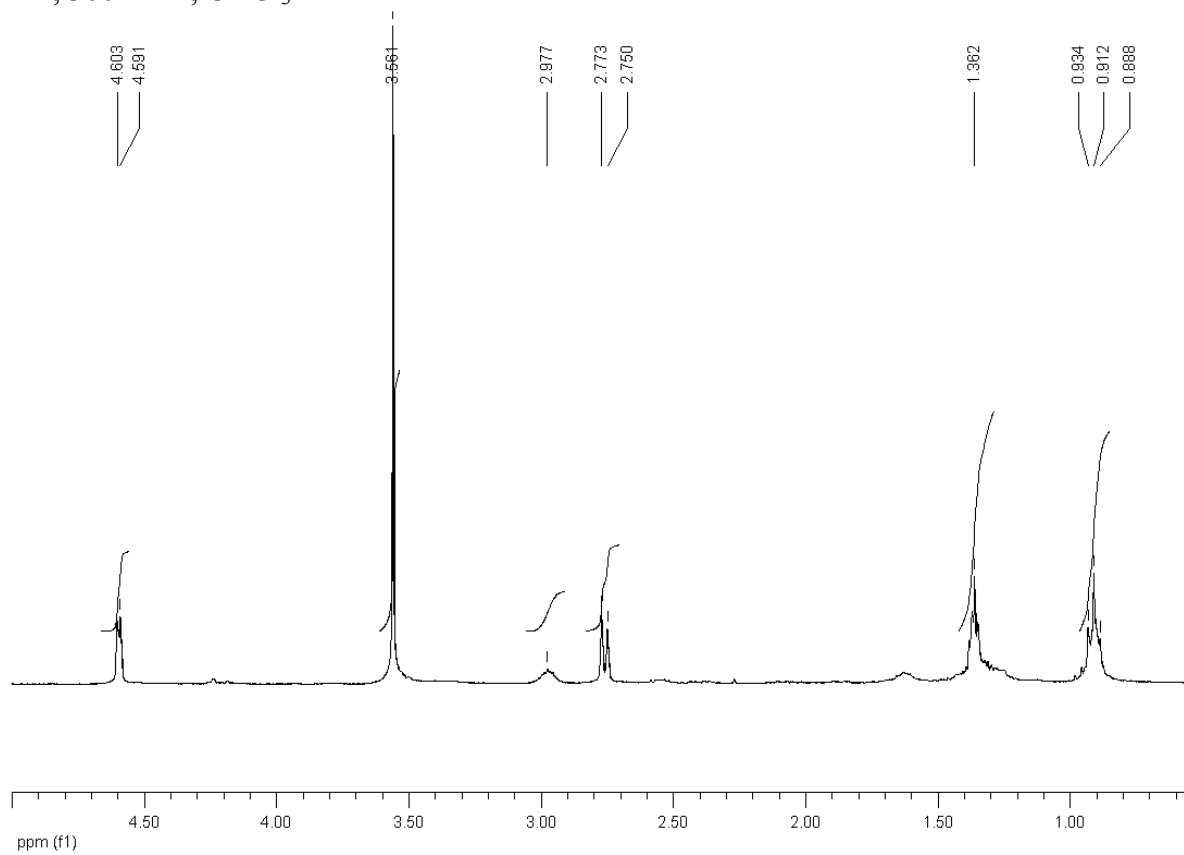


^{13}C APT NMR, 75 MHz, CDCl_3

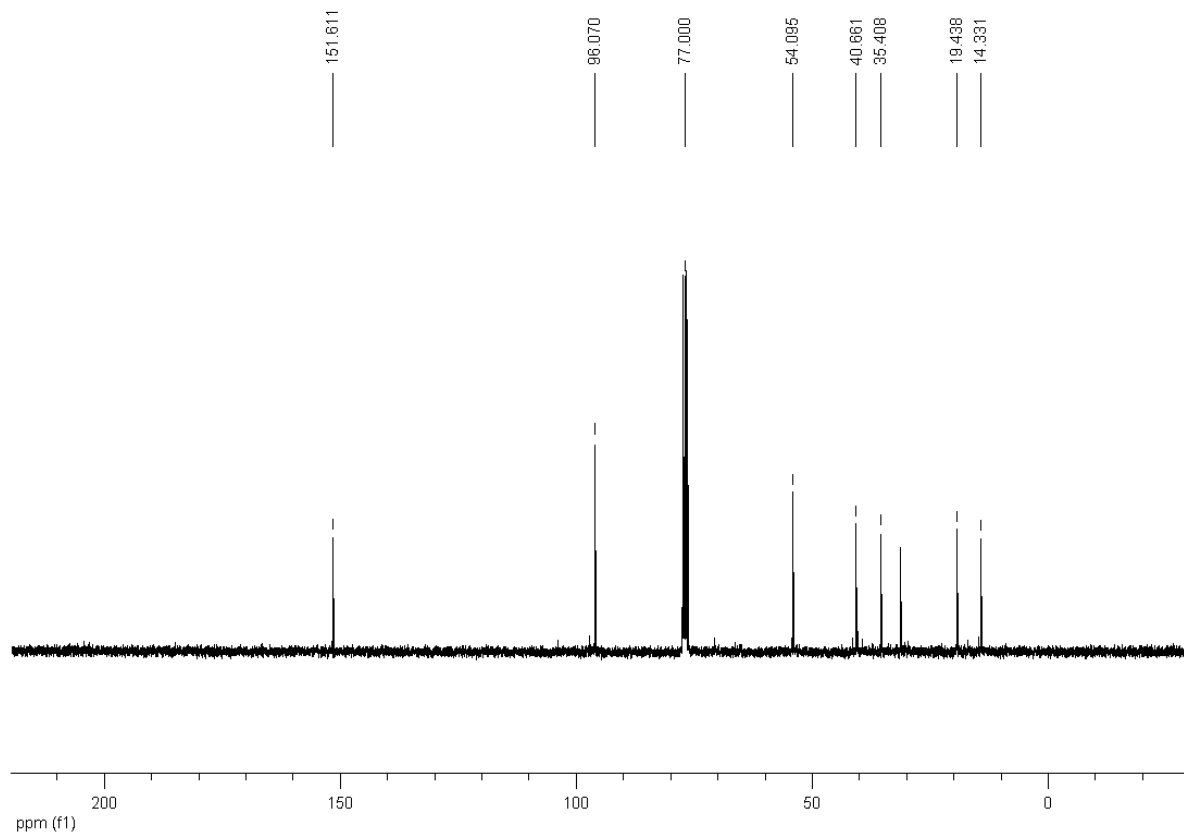


1,5-dimethoxy-3-propylcyclohexa-1,4-diene (4d)

^1H NMR, 300 MHz, CDCl_3

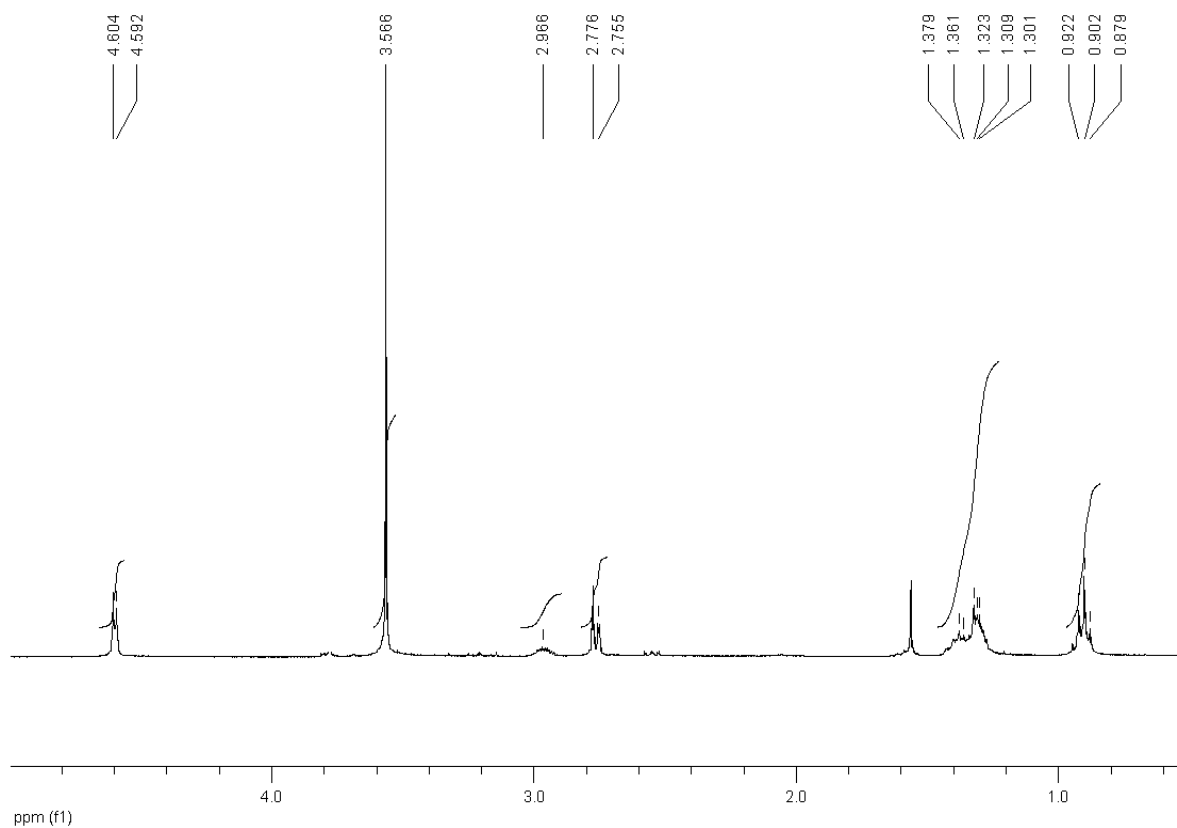


^{13}C NMR, 75 MHz, CDCl_3

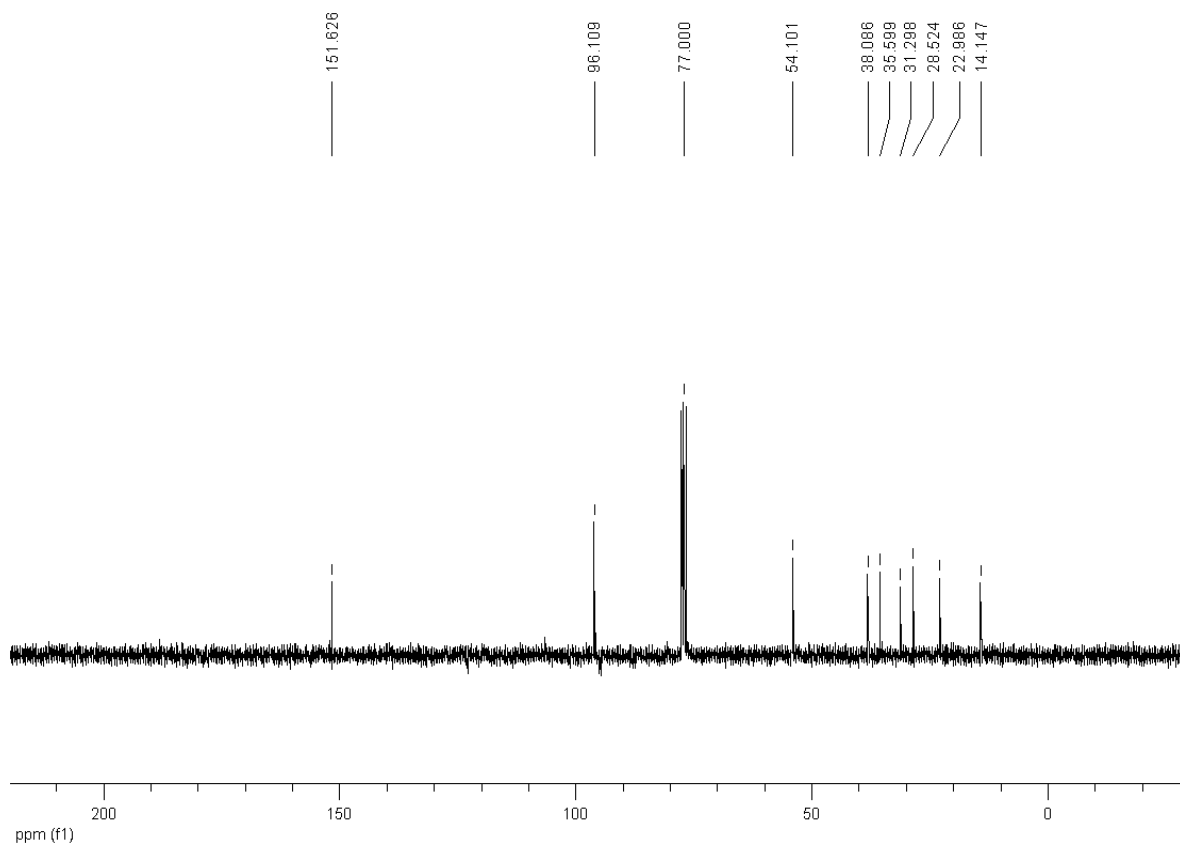


1,5-dimethoxy-3-butylcyclohexa-1,4-diene (4e)

¹H NMR, 300 MHz, CDCl₃



^{13}C NMR, 75 MHz, CDCl_3



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