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Efficient synthesis of [$^2H_2$]-tetrahydrodicranenone B and a 3-oxa-analogue resistant against β-oxidation

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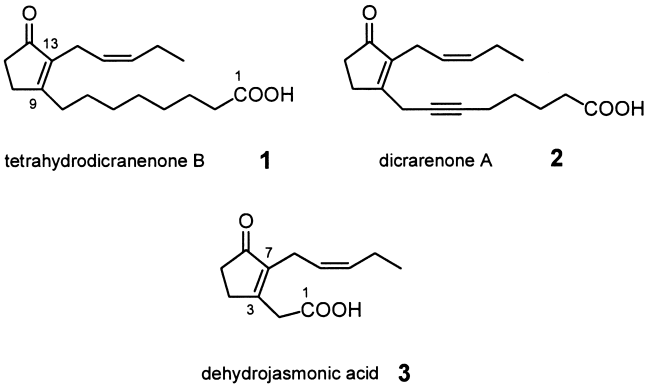
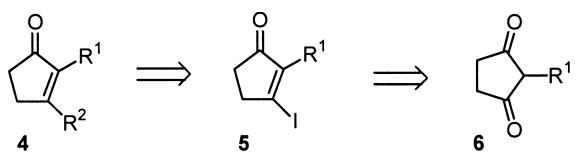
Abstract—A short efficient synthesis of two analogues of tetrahydrodicranenone B as well as a formal synthesis of tetrahydrodicranenone B (**1**) itself has been devised. The approach is based on an addition/elimination sequence of in situ prepared organocuprates to the iodocyclopentenone (**9**). The procedure is compatible with functionalised substituents.

1. Introduction

Cyclopentenone natural products are found in both animals and plants and often possess high biological activities. A typical example is tetrahydrodicranenone B (**1**), which is an antimicrobial and antihypertensive oxylipin found in Japanese mosses along with the acetylene dicranenone A (**2**) and related structures.[1–3] **1** is also known as a rearrangement product of 12-oxophytodienoic acid (12-OPDA), resulting from acid- or base-catalysed double bond migration from the 10,11 to the 9,13 position.[4] 12-OPDA is an early precursor of the plant stress hormone jasmonic acid (JA). Structurally related is 3,7-dehydrojasmonic acid (**3**) which has been isolated from *Vicia faba* fruits.[5] Formally **3** is obtained from **1** by three cycles of β-oxidation. An alternative biosynthetic route to **3** requires hydroxylation of JA at C(3) followed by elimination of water. The acid is a direct precursor of the flower fragrance *cis*-jasmone which originates from **3** by spontaneous decarboxylation after protonation of the keto group.[6]



Four principal synthetic approaches to **1** have proven successful,[7–11] yet they all are lengthy and require from 7 to 14 steps. We saw **1** as an opportunity to exploit the strategy of tandem 1,4-addition/elimination of an organometallic nucleophile to the 3-iodocyclopent-2-en-1-one (**5**) which formally represents a vinylogous acyl iodide (Scheme 1). In particular, organocuprates have been successfully employed for this strategy and made short routes to 2,3-disubstituted cyclopentenones possible.[12–14] Other approaches utilised Pd(0) catalysts and organotin reagents for alkylation.[15,16] In this way, for example, prostaglandin PGB_1 and coriolic acid were obtained in few steps and good overall yield.[17]



Scheme 1. Retrosynthetic analysis of 2,3-disubstituted cyclopentenones.

Keywords: natural products; tetrahydrodicranenone B; cyclopentenones; organocuprates; organozincates.

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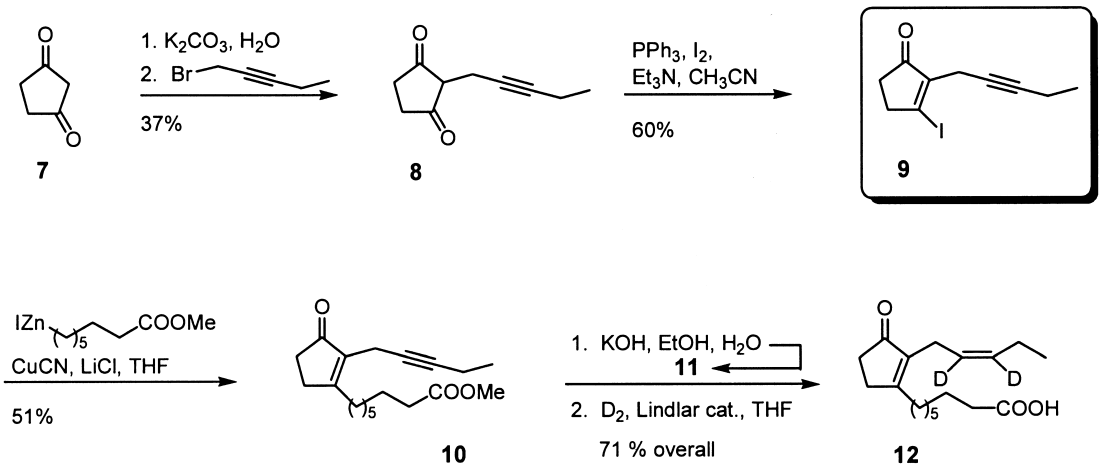


Scheme 2. Synthesis of deuterium-labelled tetrahydrodicranenone B (**12**).

The vinyl iodide of type **5** can be obtained from **6** by direct iodination,[17] and as an alkylated 1,3-diketone **6** is easily available by a number of different routes.[18] Following this principal approach, three simple operations are sufficient to establish the basic framework of the title compound **1** which we envisaged as a readily available and stable (no double bond migration) internal standard for gas chromatographic quantification of the phytohormone 12-OPDA. Moreover, the same route can be used to prepare other bioactive cyclopentenenones such as **3** or analogues of **1** that are resistant towards β-oxidation and, hence, showing the in planta effects of the genuine oxylipin, minimising effects of metabolites of this molecule.

2. Results and discussion

The success of the approach outlined in Scheme 1 was first demonstrated by the synthesis of deuterium-labelled tetrahydrodicranenone B (**1**). Commercial 1,3-cyclopentanedione (**7**) was first alkylated with 1-bromo-pent-2-yne. Side products resulted from significant *O*-alkylation or multiple alkylations. Conducting the reaction in water and an optimised work up gave the desired compound **8** in 37% yield along with unreacted starting material (Scheme 2). This mixture was treated with Ph_3P and iodine[19] to give the key intermediate **9**. Chromatographic purification furnished pure **9** in 60% yield. The second side chain was introduced via an organocopper reagent, prepared in situ from an organozinc precursor.[20]

The organozinc reagent was made from methyl 8-iodooctadecanote[21] and zinc activated with 1,2-dibromoethane and trimethylsilyl chloride according to Knochel's method.[22] It was reacted with cycloalkenyl iodide **9** after transmetallation to copper and resulted in a 51% yield of compound **10**. The mechanism[23] for this reaction is a 1,4-conjugate addition followed by elimination of iodide to give the desired compound **10**. The alternative route, employing $Pd(Ph_3)_2Cl_2$ as a catalyst for alkylation gave, however, only a 28% yield, with the primary side reaction being transmetallation, which transformed the vinyl iodide into an alkenyl-zinc compound. With the intact carbon skeleton completed, deuterium-labelled tetrahydrodicranenone B (**12**) was obtained in 71% overall yield after saponification (KOH, aq. EtOH, 74%) and reduction ($^2H_2$ gas) with Lindlar's catalyst (95%).[11]

To provide an inert (stable towards β-oxidation) analogue of tetrahydrodicranenone B with possibly interesting biological activity, we also synthesised the 3-oxa-analogue **16** (Scheme 3(b)). The required side chain building block **14** was obtained in two steps[24] from 5-chloropentanol (**13**) as shown in Scheme 3(a).

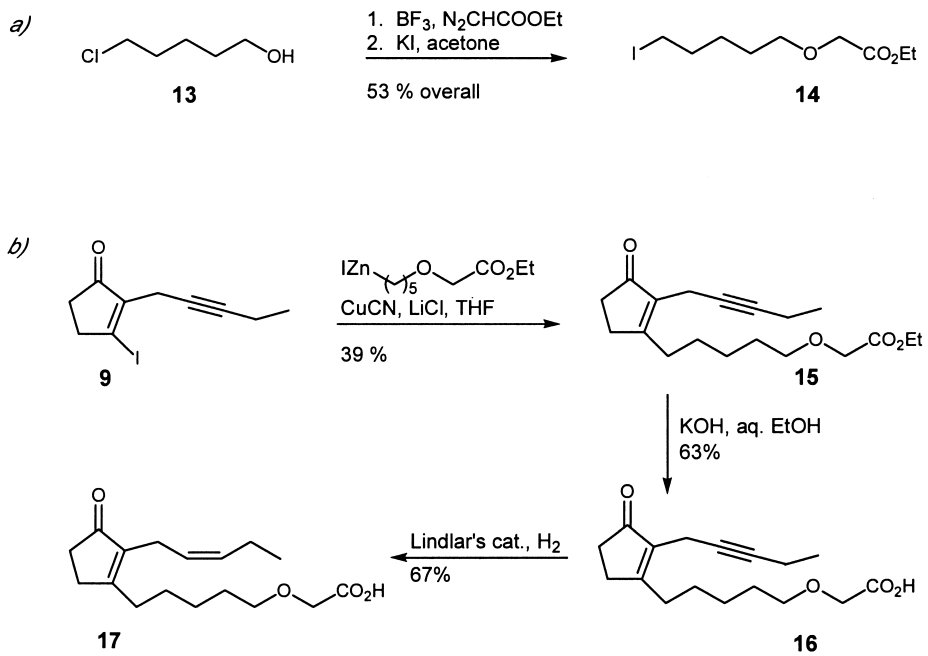
The ω-iodo ester **14** was transformed into the corresponding organozinc compound as above (Scheme 2) and, after transmetallation to copper, was reacted with **9** to give **15**. Ester hydrolysis and semi-hydrogenation (Lindlar's catalyst, H_2) completed the synthesis.

$^2H_2$-dihydrodicrarenone B (**12**) proved to be well suited as an internal standard for the quantification of 12-OPDA in damage- or herbivore-induced plants by GC–MS. The typical peak splitting and broadening of the methyl ester of 12-OPDA, which is due to double bond migration from the 10,11- to the more stable 9,13 position, does not occur. Moreover, owing to the two deuterium atoms in [$^2H_2$]-**12** a reliable mass spectroscopic quantification of the internal standard is possible, even, if large amounts of natural 12-OPDA with the same molecular weight as tetrahydrodicranenone (**1**), are present. The profile of biological activities of **12** and **17** as elicitors of plant secondary metabolism, analogous to 12-OPDA,[25,26] is currently being evaluated.

3. Experimental

3.1. General

Reactions were performed under Ar. THF was dried over potassium/benzophenone and acetonitrile over phosphorous pentoxide. High resolution gas chromatography/mass spectrometry was performed on a Micromass MasSpec (Micromass, Manchester, UK) double-focusing magnetic sector mass spectrometer (geometry EBE) connected to a Hewlett Packard HP6890 II gas chromatograph, equipped with an DB-5 (J&W Scientific) non-polar capillary column (30 m×0.25 mm, 0.25 μm). IR: Bruker Equinox 55 FTIR



Scheme 3. Synthesis of the 3-oxo analogue **17** of tetrahydrodicranenone B.

Spectrophotometer. ^{1}H and ^{13}C NMR: Bruker Avance 400 spectrometer (Bruker, D-76287 Rheinstetten/Karlsruhe, Germany). Chemical shifts of ^{1}H and ^{13}C NMR are given in ppm (δ) based on solvent peaks.

3.1.1. 2-Pent-2-ynyl-cyclopentane-1,3-dione (8). To a solution of K_2CO_3 (8.3 g, 60 mmol) in water (60 ml) was slowly added 1,3-cyclopentanedione (5.6 g, 57 mmol). The solution was heated to 60°C and stirred as 1-bromo-2-pentyne (8.6 g, 58 mmol) was added dropwise. After stirring for 24 h at 60°C, the reaction mixture was allowed to cool to rt and aq. 1N NaOH was added until a pH of 12 was reached. The mixture was extracted with ether (3x). The aqueous layer was chilled, and conc. aq. HCl was slowly added until pH 1 was reached. The product was extracted with of chloroform, dried over Na_2SO_4, and the solvent removed under low pressure to give 3.5 g (35%) of a tan solid that was used for subsequent reactions without further purification. MS (EI 70 eV) *m/z*: 164 (M^+, 100), 149 (98), 135 (53), 121 (18), 107 (25), 98 (5), 91 (10), 79 (27), 77 (20), 65 (9), 55 (21); exact mass 164.0837; calcd for $C_{10}H_{12}O_2$ 164.0837.

3.1.2. 3-Iodo-2-pent-2-ynyl-cyclopent-2-enone (9). To a stirred solution of triphenylphosphine (1.18 g, 4.5 mmol) in dry acetonitrile (40 ml) was added iodine (1.139 g, 4.5 mmol) in one portion. This was stirred at rt for 2 h, after which 2-pent-2-ynyl-cyclopentane-1,3-dione (0.65 g, 4 mmol) was added in one portion followed by immediate addition of triethylamine (0.61 ml, 0.44 g, 4.3 mmol). The reaction was heated to 75°C for 45 min, stirred overnight at rt, and then at 85°C for 1 h. After cooling to rt, ether was used to wash the reaction mixture into flask containing about 3 g celite 545. The solvent was removed under low pressure and the solids were loaded onto a silica gel column. Elution with petrol ether/ethyl acetate (4:1, v/v) afforded a slightly yellow oil that solidified. Yield: 0.65 g (60%). mp: 40.5–42.2°C. ^{1}H NMR (400 MHz, $DCCl_3$) δ 1.09 (t, J=7.55 Hz, 3H), 2.12 (qrt of t, J=7.4, 2.51 Hz, 2H), 2.54 (m, 2H), 3.02 (m, 2H), 3.12 (sept, J=1.21 Hz, 2H). ^{13}C NMR (100 MHz, $DCCl_3$) δ 12.59, 14.07, 17.47, 36.72, 39.51, 73.43, 82.55, 134.78, 147.27, 201.26. IR (KBr, neat) 3371, 2979, 2939, 2913, 1696, 1611, 1429, 1410, 1320, 1275, 1190, 1039, 972, 921, 816 cm^{-1}. MS (EI 70 eV) *m/z* (%) 274 (M^+, 100), 259 (45), 147 (57), 132 (18), 119 (7), 105 (37), 91 (23), 79 (17), 77 (25), 65 (10); exact mass 273.9855; calcd for $C_{10}H_{11}IO$ 273.9855.

3.1.3. Methyl 8-(3-oxo-2-pent-2-ynyl-cyclopent-1-enyl)-octanoate (10). In a 25 ml flask was placed Zn powder (330 mg, 5 mmol) and THF (0.5 ml). The suspension was heated to 60°C as 1,2-dibromoethane (0.02 ml) was added. After stirring at this temperature for about 5 min, the reaction was allowed to cool to rt and trimethylsilyl chloride (0.02 ml) was added with stirring, followed after 15 min by a solution of methyl 8-iodo-octanoate (680 mg, 2.4 mmol) in THF (0.6 ml). The mixture was maintained for 1.5 h at 30°C. Then, stirring and heating were stopped and the Zn powder was allowed to settle. The supernatant was transferred to a flask containing CuCN (0.16 g, 1.8 mmol) and LiCl (0.14 g, 3.3 mmol, dried for 1 h at 140°C under high vacuum) in THF (1 ml) at −20°C. After 10 min the mixture was cooled to −60°C and 3-iodo-2-pent-2-ynyl-cyclopent-2-enone (208 mg, 0.76 mmol) in THF (0.8 ml) was added. The mixture was slowly allowed to warm to rt overnight and hydrolysed by aq. NH_4Cl. Ether was added and the biphasic mixture was filtered. The organic layer was washed with water, aq. satd NaCl, dried over Na_2SO_4, and the solvent removed under low pressure. The residue was purified by flash chromatography with silica gel using petrol ether/ethyl acetate (4:1, v/v) to give the product as a yellow tinted liquid. Yield: 117 mg (51%). ^{1}H NMR (400 MHz, $DCCl_3$) δ 1.08 (t, J=7.56 Hz, 3H), 1.35 (m, 6H), 1.61 (m, 4H), 2.13 (qrt of t, J=7.47, 2.52 Hz, 2H), 2.30 (t, J=7.56 Hz, 2H), 2.37 (m, 2H), 2.54 (m, 4H), 3.04 (s, 2H), 3.66 (s, 3H). ^{13}C NMR (100 MHz, $DCCl_3$) δ 12.57, 12.83,

14.19, 25.03, 27.35, 29.16, 29.22, 29.52, 29.72, 31.48, 34.13, 34.17, 51.55, 75.87, 81.56, 136.31, 174.26, 175.69, 208.14. IR (NaCl) 2934, 2857, 1739, 1700, 1642, 1437, 1363, 1321, 1249, 1200, 1172, 1120, 1039, 725 cm^{-1}. MS (70 eV) (%) 304 (86), 289 (22), 275 (17), 203 (6), 189 (10), 175 (60), 161 (100), 147 (16), 133 (27), 105 (20), 91 (27), 79 (13); exact mass 304.2044; calcd for $C_{19}H_{28}O_3$ 304.2039.

3.1.4. 8-(3-Oxo-2-pent-2-ynyl-cyclopent-1-enyl)-octanoic acid (11). A cold (0°C) solution of methyl 8-(3-oxo-2-pent-2-ynyl-cylcopent-1-enyl)-octanoate (174 mg, 0.57 mmol) in ethanol (20 ml) was slowly treated with stirring with aq. KOH (0.76 g) in water (6 ml) at which the colour of the solution turned to orange. After stirring for 24 h at rt, the reaction mixture was poured into ether and water. The ether layer was washed with aq. KOH and the combined aqueous layers were acidified with conc. HCl. The product was extracted into ether and the organic layer washed with water and aq. satd NaCl. After drying over Na_2SO_4 and removing the solvent under low pressure, the residue was purified by flash chromatography with silica gel using petrol ether/ethyl acetate (2:1, v/v) with 2% acetic acid. The product was slightly yellow oil that solidified upon refrigeration. Yield: 123 mg (74%); mp 64.4–66.2°C. ^{1}H NMR (400 MHz, $DCCl_3$) δ 1.08 (t, J=7.54 Hz, 3H), 1.37 (s, 6H), 1.61 (m, 4H), 2.11 (m, 2H), 2.37 (m, 4H), 2.55 (m, 4H), 3.05 (s, 2H). ^{13}C NMR (100 MHz, $DCCl_3$) δ 12.57, 12.84, 14.19, 24.79, 27.35, 29.07, 29.21, 29.56, 29.70, 31.49, 33.93, 34.15, 75.87, 81.61, 136.34, 175.90, 178.72, 208.36. IR (NaCl, neat) 2977, 2934, 2858, 2641, 1704, 1633, 1456, 1437, 1367, 1318, 1286, 1240, 1212, 1120, 939, 819, 724 cm^{-1}. MS (70 eV) 290 (89), 275 (38), 261 (25), 247 (7), 203 (7), 189 (9), 175 (41), 161 (100), 147 (21), 133 (29), 119 (17), 105 (22), 91 (27); exact mass 290.1882; calcd for $C_{18}H_{26}O_3$ 290.1882.

3.1.5. $^2H_2$-Tetrahydrodicranenone B (12). Lindlar's catalyst (75 mg, Fluka) was placed in a dry flask and several cycles of evacuation and introduction of deuterium were performed. Following this, a balloon with deuterium was used to keep a slight positive pressure on the system and THF (1.5 ml) was added. Quinoline (17 μl) was added via syringe, followed by 8-(3-oxo-2-pent-2-ynyl-cyclopent-1-enyl)-octanoic acid (41 mg, 0.14 mmol). The mixture was stirred at room temperature until GC–MS showed complete conversion of starting material (2 h). The reaction mixture was then filtered and the filter washed generously with ether. The organic layer was washed with 2N HCl, and satd aq. NaCl. After drying over Na_sSO_4 and removal of solvent, 40 mg (96%) of a slightly brown oil was obtained (>90:10, *cis*/*trans*). Further purification was done with HPLC. ^{1}H NMR (400 MHz, $DCCl_3$) δ 0.99 (t, J=7.55 Hz, 3H), 1.35 (s, 6H), 1.52 (m, 2H), 1.64 (m, 2H), 2.35 (m, 4H), 2.42 (t, J=7.81 Hz, 2H), 2.49 (m, 2H), 2.92 (s, 2H). ^{13}C NMR (100 MHz, $DCCl_3$) δ 14.24, 20.62, 21.30, 24.77, 27.49, 29.05, 29.16, 29.37, 29.67, 31.44, 33.95, 34.35, 139.43, 174.43, 178.84, 209.64. IR (NaCl, neat): 2932, 2858, 2652, 2248, 2217, 1699, 1628, 1462, 1440, 1410, 1361, 1285, 1245, 1211, 1180, 1119, 1059, 818, 725 cm^{-1}. MS (70 eV) (%) 294 (M^+ 60), 276 (14), 247 (18), 219 (20), 205 (5), 191 (7), 179 (100), 166 (22), 151 (89), 135 (22), 123 (31), 110 (12), 93 (21), 79 (19), 69 (11); exact mass 294.2162; calcd for $C_{18}H^2_{28}H_2O_3$ 294.2164.

3.1.6. Ethyl (5-iodopentoxy)-acetate (14). (a) A chilled and well stirred solution of 5-chloro-1-pentanol (6.1 g, 50 mmol) in dichloromethane (50 ml) was treated with ethyl diazo acetate (5.7 g, 50 mmol). A few drops (~6) of boron trifluoride etherate were added to catalyse the reaction. The mixture was allowed to warm to rt and was stirred for 24 h as N_2 was given off. The reaction mixture was then poured into satd aq. $NaHCO_3$ solution. The water layer was extracted with dichloromethane and the combined organic fractions dried over Na_2SO_4. The solvent was removed under low pressure and the crude product was purified by distillation under vacuum. One main portion was obtained at 10 mbar and 120–126°C. Yield: 6.45 g (62%), colourless oil.

(b) A stirred suspension of NaI (12 g, 80 mmol) in dry acetone (50 ml) was treated with ethyl (5-chloro-pentoxy)-acetate (4.0 g, 19 mmol). After 2 days of stirring at room temperature, followed by 7 h at reflux, the reaction mixture was diluted with ether and filtered through a layer of celite. The solvent was removed and the residue was purified by flash chromatography over silica gel using ethyl acetate/petrol ether (1:3, v/v). The product was collected as a slightly orange liquid. Yield: 4.96 g (86%). ^{1}H NMR (400 MHz, $DCCl_3$) δ 1.27 (3H, t, J=7.52 Hz), 1.48 (2H, m), 1.61 (2H, m), 1.84 (2H, qnt, J=7.38 Hz), 3.17 (2H, t, J=7.04 Hz), 3.51 (2H, t, J=6.42 Hz), 3.04 (2H, s), 4.19 (2H, qrt, J=7.15 Hz). ^{13}C NMR (100 MHz, $DCCl_3$) δ 6.87, 14.32, 27.14, 28.58, 33.34, 60.89, 68.44, 71.54, 170.59. IR (NaCl, film) 2984, 2940, 2864, 1755, 1734, 1473, 1446, 1424, 1375, 1272, 1201, 1136, 1027, 929, 859, 723 cm^{-1}. MS (70 eV) (%) 227 (2), 197 (19), 173 (25), 155 (13), 105 (28), 88 (28), 69 (100); exact mass 226.9939; calcd for $C_6H_{12}OI$ [$M-CO_2CH_2CH_3$] 226.9933.

3.1.7. [5-(3-Oxo-2-pent-2-ynyl-cyclopent-1-enyl)-pentyl-oxy]-acetic acid ethyl ester (15). The alkylation of **9** was done as described for **10**. A suspension of Zn dust (660 mg) in THF (1 ml) was stirred at 60°C as dibromoethane (0.04 ml) was added. After 5 min at 60°C, the mixture was cooled to rt and trimethylsilyl chloride (0.04 ml) was added. This was stirred at rt for 15 min, then heated 30°C followed by addition of ethyl (5-iodo-pentoxy)-acetate (1.33 g, 4.4 mmol) in THF (1.2 ml). Stirring was continued for 1.5 h at 30°C and, then, Zn dust was allowed to settle. The supernatant was taken up in a syringe and added to a stirred mixture of LiCl (0.28 g, 6.6 mmol, dried at 140°C for 1 h under high vacuum) and CuCN (0.32 g, 3.6 mmol) in 2 ml THF at −20°C. Stirring was continued for 15 min at −20°C, then at −78°C (very viscous solution) followed by addition of 3-iodo-2-pent-2-ynyl-cyclopent-2-enone (560 mg, 2.0 mmol), dissolved in dry in THF (1.6 ml). This was left to warm to rt resulting in a deep red solution. The solution was chilled and aq. NH_4Cl and ether were added. This biphasic mixture was filtered carefully into a separatory funnel. More ether and water were added, and the ether layer was washed with water and satd aq. NaCl. After drying (Na_2SO_4) and removal of solvent, the residue was purified by flash chromatography over silica gel using ethyl acetate/petrol ether (1:3, v/v) for elution. Yellow liquid. Yield: 255 mg (39%). ^{1}H NMR (400 MHz, $DCCl_3$) δ 1.07

(3H, t, J=7.56 Hz), 1.27 (3H, t, J=7.04 Hz), 1.46 (2H, m), 1.64 (5H, m), 2.10 (2H, qrt of t, J_{qrt}=7.5, 2.5 Hz), 2.37 (2H, m), 2.51 (2H, m), 2.57 (2H, t, J=7.8 Hz), 3.04 (2H, s), 3.53 (2H, t, J=6.42 Hz), 4.04 (2H, s), 4.20 (2H, qrt, J=7.12 Hz). ^{13}C NMR (100 MHz, $DCCl_3$) δ 12.54, 12.80, 14.16, 14.33, 26.39, 27.19, 29.49, 29.54, 31.41, 34.12, 60.88, 68.53, 71.75, 75.84, 81.57, 136.37, 170.61, 175.53, 208.13. IR (NaCl, film) 2976, 2973, 2862, 1755, 1699, 1641, 1435, 1366, 1280, 1203, 1137, 1034, 939, 856, 720 cm^{-1}. MS (70 eV) (%) 320 (M^+, 63), 305 (9), 291 (21), 247 (16), 233 (53), 216 (29), 201 (36), 187 (22), 175 (77), 161 (100), 145 (23), 133 (33), 105 (28), 91 (37), 69 (51); exact mass 320.1985; calcd for $C_{19}H_{28}O_4$ 320.1988.

3.1.8. [5-(3-Oxo-2-pent-2-ynyl-cyclopent-1-enyl)-pentyl-oxy]-acetic acid (16). A well stirred and chilled solution of **15** (105.8 mg) in ethanol (10 ml) was treated with KOH in water (2.5 ml, 1.8 M solution) and the reaction was allowed to warm to rt overnight. The reaction mixture was washed with ether and acidified with conc. HCl. The product was extracted into ether. Drying (Na_2SO_4), removal of solvent removed and purification by silica gel flash chromatography with petrol ether/ethyl acetate (2:1, v/v) containing 2% acetic acid afforded the product as slightly yellow oil. Yield: 61 mg (63%). ^{1}H NMR (400 MHz, $DCCl_3$) δ 1.07 (3H, t, J=7.42 Hz), 1.46 (2H, m), 1.65 (4H, m), 2.12 (2H, m), 2.40 (2H, m), 2.53 (2H, m), 2.58 (2H, t, J=7.82 Hz), 3.05 (2H, s), 3.57 (2H, t, J=6.54 Hz), 4.11 (2H, s). ^{13}C NMR (100 MHz, $DCCl_3$) δ 12.55, 12.79, 14.19, 20.82, 26.29, 27.16, 29.43, 29.53, 31.41, 34.12, 67.96, 71.85, 75.77, 81.62, 136.39, 175.95, 208.66. IR (NaCl, film) 2977, 2938, 2867, 2632, 2543, 1755, 1729, 1699, 1630, 1435, 1367, 1320, 1212, 1134, 1041, 939, 876, 664 cm^{-1}. MS (70 eV) (%) $C_{18}H_{28}O_3$; exact mass 292.1674; calcd for $C_{17}H_{24}O_4$ 292.1675.

3.1.9. [5-(3-Oxo-2-pent-2-enyl-cyclopent-1-enyl)-pentyl-oxy]-acetic acid (17). Lindlar's catalyst (54 mg) was placed in a flask with a magnetic stir bar under Ar. This was taken through several cycles of evacuation and hydrogen purge. After the final purge, THF (1.5 ml) and quinoline (10 μl) were added. Then, the acid **16** (29 mg) was added and the mixture stirred for 25 min. The reaction mixture was filtered into a sep funnel with ether and 2N HCl. The ether layer was washed with 2N HCl and satd aq. NaCl, dried over Na_2SO_4, and removed under low pressure to give 19.4 mg (67%) of a colourless oil. ^{1}H NMR (400 MHz, $DCCl_3$) δ 0.98 (3H, t, J=7.44 Hz), 1.42 (2H, m), 1.56 (2H, qrt, J=7.68 Hz), 1.67 (2H, qrt, J=7.05 Hz), 2.14 (2H, qrt, J=7.56 Hz), 2.37 (2H, m), 2.44 (2H, t, J=7.68 Hz), 2.49 (2H, m), 2.92 (2H, d, J=7.04 Hz), 3.56 (2H, t, J=6.42 Hz), 4.10 (2H, s), 5.20 (1H, m), 5.36 (1H, m). ^{13}C NMR (100 MHz, $DCCl_3$) δ 14.28, 20.74, 21.37, 26.28, 27.33, 29.32, 29.39, 31.36, 34.31, 67.99, 71.82, 125.42, 132.46, 139.47, 174.36, 209.83. IR (NaCl, film) 3010, 2935, 2863, 2539, 1735, 1695, 1650, 1624, 1556, 1431, 1406, 1362, 1204, 1135, 1050, 941, 864, 675 cm^{-1}. MS (70 eV) (%) 294 (50), 265 (12), 235 (56), 219 (6), 189 (12), 177 (77), 164 (31), 149 (100), 135 (27), 121 (24), 105 (25), 91 (33), 79 (34); exact mass 294.1831; calcd for 294.1831.

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References

1. Ichikawa, T.; Namikawa, M.; Yamada, K.; Sakai, K.; Kondo, K. *Tetrahedron Lett.* **1983**, *24*, 3337–3340.
2. Sakai, K.; Fujimoto, T.; Yamashita, M.; Kondo, K. *Tetrahedron Lett.* **1985**, *26*, 2089–2092.
3. Ichikawa, T.; Yamada, K.; Sakai, K.; Kondo, K. 47th Annual Meeting Chem. Soc. Japan, Kyoto, Japan, 1983, p 1117.
4. Beal, M. H.; Ward, J. L. *Nat. Prod. Rep.* **1998**, *15*, 533–548.
5. Miersch, O.; Sembdner, G.; Schreiber, K. *Phytochemistry* **1989**, *28*, 339–340.
6. Koch, T.; Bandemer, K.; Boland, W. *Helv. Chim. Acta* **1997**, *80*, 838–850.
7. Trost, B. M.; Pinkerton, A. B. *Org. Lett.* **2000**, *2*, 1601–1603.
8. Trost, B. M.; Pinkerton, A. B. *J. Org. Chem.* **2001**, *66*, 7714–7722.
9. Moody, C. J.; Roberts, S. M.; Toczek, J. *J. Chem. Soc. Chem. Commun.* **1986**, 1292–1293.
10. Casey, G.; Taylor, R. J. *Tetrahedron* **1989**, *45*, 455–466.
11. Lis, L.; Pap, A.; Zheldakova, T.; Borisov, E.; Lakhvich, F. *J. Org. Chem. USSR* **1991**, *27*, 1889–1900.
12. Bradbury, R. H.; Gilchrist, T. L.; Rees, C. W. *J. Chem. Soc., Perkin Trans. 1* **1981**, *12*, 3234–3238.
13. Piers, E.; Cheng, K. F.; Nagakura, I. *Can. J. Chem.* **1982**, *60*, 1256–1263.
14. Piers, E.; Banville, J.; Lau, C. K.; Nagakura, I. *Can. J. Chem.* **1982**, *60*, 2965–2975.
15. Duan, J.-P.; Cheng, C.-H. *Tetrahedron Lett.* **1993**, *34*, 4019–4022.
16. Gilchrist, T. L.; Summersell, R. J. *Tetrahedron Lett.* **1987**, *28*, 1469–1472.
17. Stille, J. K.; Sweet, M. P. *Tetrahedron Lett.* **1989**, *30*, 3645–3648.
18. Schick, H.; Lehmann, G.; Hilgetag, G. *Angew. Chem. Int. Ed.* **1967**, *6*, 80–81.
19. Piers, E.; Grierson, J. R.; Lau, C. K.; Nagakura, I. *Can. J. Chem.* **1982**, *60*, 210–223.
20. Knochel, P.; Almenea Parea, J. J.; Jones, P. *Tetrahedron* **1998**, *54*, 8275–8319.
21. Kling, M. R.; Easton, C. J.; Poulos, A. *J. Chem. Soc., Perkin Trans. 1* **1993**, *10*, 1183–1190.
22. Knochel, P.; Yeh, M. C. P.; Berk, S. C.; Talbert, J. *J. Org. Chem.* **1988**, *53*, 2390–2392.
23. Erdik, E. *Organozinc Reagents in Organic Synthesis*. CRC: Boca Raton, FL, 1996.
24. Buchanan, G. W.; Gerzain, M.; Bensimon, C.; Ellen, R.; Reynolds, V. M. *J. Mol. Struct.* **1997**, *404*, 307–317.
25. Blechert, S.; Bockelmann, C.; Füsslein, M.; von Schrader, T.; Stelmach, B.; Niesel, U.; Weiler, E. W. *Planta* **1999**, *207*, 470–479.
26. Ichihara, A.; Toshima, H. In *Biologically Active Natural Products: Agrochemicals*. Cutler, H. G., Cutler, S. J., Eds.; CRC: Boca Raton, FL, 1999; p 93 and references cited therein.