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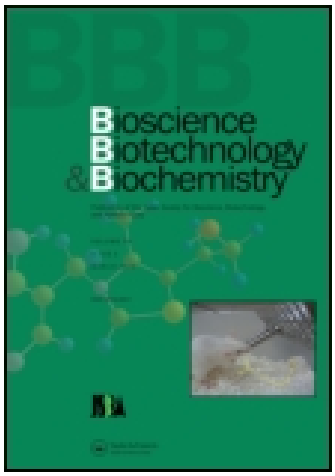

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Efficient Syntheses of the OPC Homologous Series, OPC-1:0, -3:0, -4:0, -5:0, -6:0, -7:0, and-8:0

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Efficient Syntheses of the OPC Homologous Series, OPC-1:0, -3:0, -4:0, -5:0, -6:0, -7:0, and -8:0

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Received April 25, 1997

The OPC homologous series was synthesized from 2-[(*Z*)-2-pentenyl]cyclopenten-1-one in short steps and with high yields. The carbon–carbon bond formation was achieved by the 1,4-conjugate addition approach. This method makes it possible to supply a sufficient amount of OPC homologues which would enable significant information to be collected for plant physiological studies.

Key words: jasmonoid; octadecanoid; 12-oxo-PDA; OPC; 1,4-conjugate addition

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Jasmonoids have recently been postulated as a class of plant hormones.[1] Their biosynthesis is initiated from α-linolenic acid (C_{18}), and the precursor, dihydro-12-oxo-PDA (**1b**; also named OPC-8:0) undergoes three-time shortening of the two-carbon unit by β-oxidation to successively provide OPC-6:0, OPC-4:0, and OPC-2:0 (**2a**; *epi*-JA)[2] as shown in Fig. 1. 12-Oxo-PDA (**1a**)[3] and dihydro-12-oxo-PDA (**1b**) themselves, and also the long-chain homologues and oxa-analogues of **1b**, have recently been shown to exhibit biological activities in some typical bioassay systems of JA.[4] These results suggest that the early intermediates (**1a** and **1b**) of the octadecanoid signalling pathway are also biologically active without needing to be converted into **2a** by β-oxidation and that there are some independent receptors corresponding to the carbon-chain length of the signalling molecules. In connection with our study on the similarities in biological activity of coronatine (**3a**) and coronafacic acid (**3b**) to that of jasmonoids (Fig. 2),[5] we have efficiently synthesized the OPC homologous series[4a] in short steps and with high yields.

The industrial synthetic intermediate of JA, 2-[(*Z*)-2-pentenyl]cyclopenten-1-one (**4**),[6] was used as the starting materials for all the OPC homologues. The carbon–carbon bond was formed by the 1,4-conjugate addition approach.

In the synthesis of OPC-1:0, tris(phenylthio)methyl lithium was used as an ester carbanion synthon of the one-carbon unit (Scheme 1).[7a] 1,4-Conjugate addition to **4** proceeded smoothly to give **5a** (51%) and **5b** (27%), which could be separated by silica gel column chromatography. The stereochemistry of **5a** was determined by a NOESY

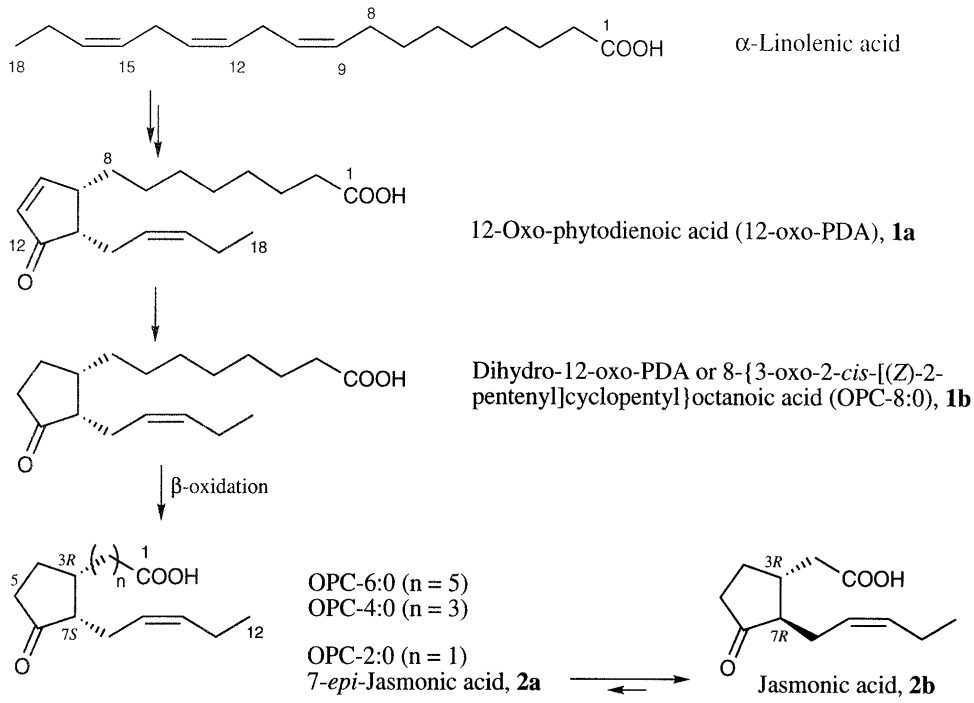

Fig. 1. Biosynthesis of Jasmonic Acid (JA) from α-Linolenic Acid.

Abbreviations: JA, jasmonic acid; PDA, phytodienoic acid; OPC-8:0, 8-{3-oxo-2-*cis*-[(*Z*)-2-pentenyl]cyclopentyl}octanoic acid; the other OPC abbreviations follow the former and their numbers indicate corresponding carboxylic acids.

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experiment. The *trans*-relationship between H-2 and H-3 in **5a** is explicable by the observed NOESY correlations (H-2/H-4α, H-3/H-4β, H-3/H-1′α, H-3/H-1′β, and H-3/H-2′). Furthermore, it was revealed that **5b** could be isomerized to **5a** by treating with sodium methoxide in a quantitative yield. This latter fact also suggests **5a** to be a thermodynamically stable *trans*-isomer. Although ethanolysis of **5a** with Hg(II) salt in refluxing ethanol[7b] gave desired product **5c** (67%) and by-product **5d** (17%), that of **5b** under the same conditions gave only **5d** (42%) and decomposed products. Ethanolysis of **5a** proceeded under milder conditions at r.t. to give **5c** (63%); however, the concurrent production of **5d** (7%) was unavoidable. Therefore, isomerization of **5b** to **5a** was required before ethanolysis. Ethyl ester **5c** was subjected to alkaline hydrolysis to give *trans*-OPC-1 : 0 (**5e**) in an 81% yield.

The other OPC homologues, from OPC-3 : 0 to OPC-8 : 0, were synthesized in the same two-step manner of 1,4-conjugate addition of zinc-copper reagents to **4** and subsequent alkaline hydrolysis.

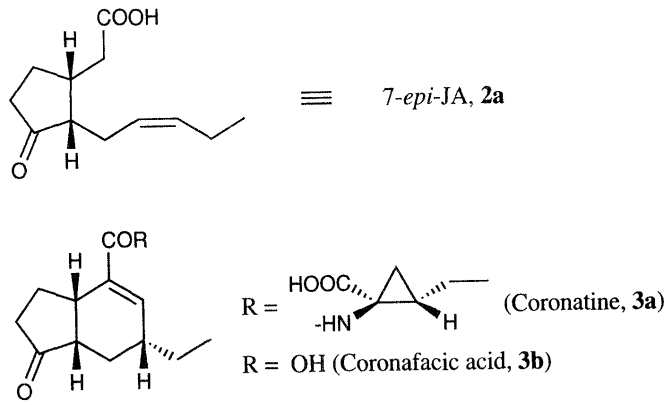
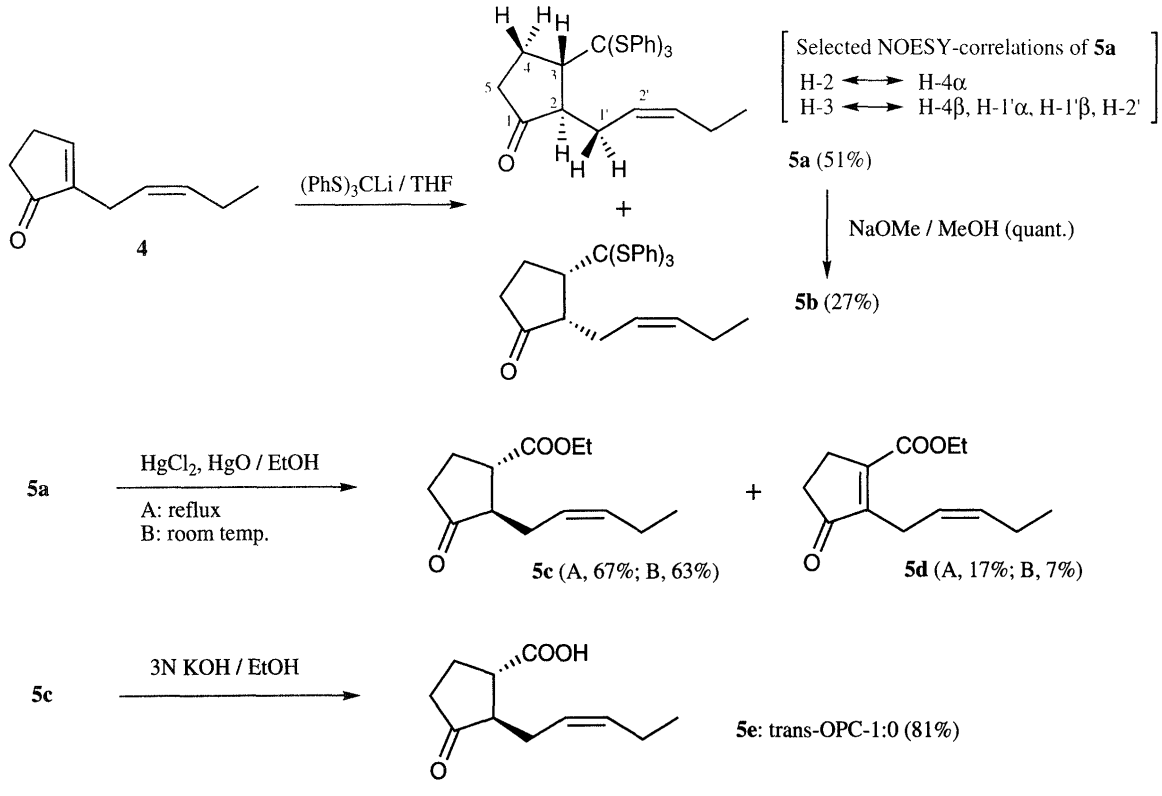


Fig. 2. Structural Similarity among JA, Coronatine, and Coronafacic Acid.

Iodo-esters (**7a–7f**) were prepared from the corresponding commercially available bromo- (**6a**, **6c–6f**) or chloro- (**6b**) esters by treating with sodium iodide in refluxing acetone.[8] Zinc–copper reagents (**8a–8f**), which had been generated from the corresponding iodo-esters (**7a–7f**) by the method of Asaoka *et al.*,[9] were subjected to 1,4-conjugate addition to **4**. In order to optimize the reaction conditions, the stoichiometry of the zinc–copper reagents and the reaction temperature were varied. It was found that the reaction proceeded rather slowly, even at r.t. Five equivalents of zinc–copper reagents was required to complete the reaction at r.t. for 36 h. These reactions gave the esters of OPC homologues (**9a–9f**) in high yields (71–83%), in spite of the carbon-chain length, as summarized in the Table. The products were obtained as an inseparable mixture of *cis*- and *trans*-isomers (containing 20–25% of *cis*-isomers), which were distinguishable based on their ^{13}C-NMR spectra. The ^{13}C-signals of *trans*-isomers at the α- and β-positions of the ketone were more downfield (*ca.* 2.4 ppm) than those of the *cis*-isomers. This same tendency has been observed in methyl jasmonate and methyl *epi*-jasmonate.[3b] Conventional alkaline hydrolysis provided the desired carboxylic acids, OPC homologues **10a–10f**, as predominantly *trans*-isomers (*ca.* >95%, based on their ^{13}C-NMR spectra as already described) in high yields (76–97%, see the Table). In this way, the OPC homologous series, which would contribute to plant physiological studies related to jasmonoids, was synthesized in short steps and with high yields. OPC-2 : 0 (JA) is, of course, commercially available.

In preliminary experiments, OPC-8 : 0 (**10f**), OPC-6 : 0 (**10d**), and OPC-4 : 0 (**10b**) exhibited cell expansion-inducing activity (with cells of potato tubers) at the same concen-



Scheme 1. Synthesis of OPC-1 : 0.

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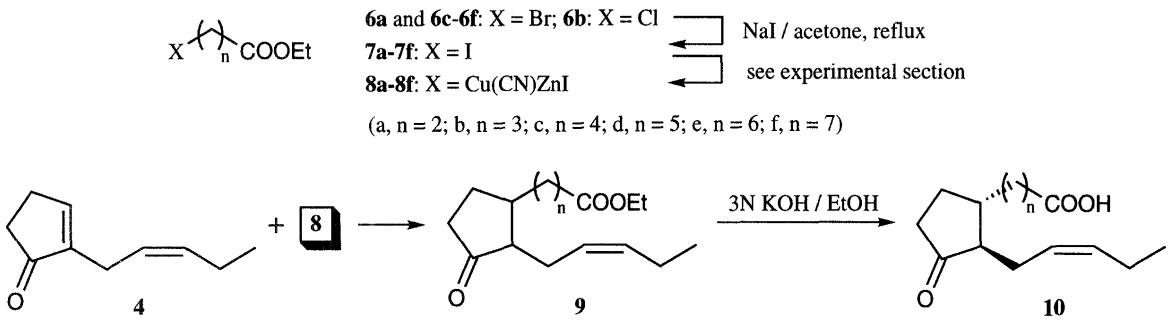

Scheme 2. Syntheses of OPC Homologues.

Table Results of 1,4-Conjugate Addition of Zinc-Copper Reagents (**8**) to Enone (**4**) and Alkaline Hydrolysis of Esters (**9**)

Zinc-copper reagents	Isolated yield	
	1,4-Conjugate addition product (%)	Alkaline hydrolysis product (%)
8a: $n=2$	**9a** (83%)	**10a**: OPC-3:0 (83%)
8b: $n=3$	**9b** (82%)	**10b**: OPC-4:0 (93%)
8c: $n=4$	**9c** (71%)	**10c**: OPC-5:0 (76%)
8d: $n=5$	**9d** (80%)	**10d**: OPC-6:0 (87%)
8e: $n=6$	**9e** (79%)	**10e**: OPC-7:0 (93%)
8f: $n=7$	**9f** (74%)	**10f**: OPC-8:0 (97%)

tration as that of JA ($>10^{-5}$ M),[10] but the odd-numbered homologues (**5e**, **10a**, **10c**, and **10e**)[11] did not exhibit such activity. Furthermore, **10f**, **10d**, and **10b** exhibited tuber-inducing activity (with single-node segments of potato stems) at the same concentration as that of JA ($>10^{-7}$ M). For example, tuberonic acid (12-hydroxyl-JA) does not exhibit cell expansion-inducing activity, although it exhibits tuber-inducing activity.[12] Therefore, the odd-numbered homologues of OPC have the potential for exhibiting certain biological activities. The other biological activities of the OPC homologous series, including the requirement or not of β-oxidation, will be evaluated, and the results will be subsequently published.

In conclusion, the OPC homologous series, OPC-1:0, -3:0, -4:0, -5:0, -6:0, -7:0, and -8:0, was synthesized from 2-[(*Z*)-2-pentenyl]cyclopenten-1-one as the common starting material in short steps and with high yields. In addition to the known even-numbered OPC homologues as biosynthetic intermediates, our syntheses provided the odd-numbered homologues which have not been isolated from plant origins.[13] Plant physiological studies related to jasmonoids will be assisted by these OPC homologues providing significant information. Furthermore, these OPC homologues are useful intermediates for the other promising compounds such as the OPC-oxa-analogues which do not undergo β-oxidation.

Experimental

General methods. ^{1}H- and ^{13}C-NMR spectra were recorded with a JEOL JNM-EX-270 spectrometer (^{1}H at 270 MHz; ^{13}C at 67.5 MHz) or with a Brucker AM-500 spectrometer (^{1}H at 500 MHz; ^{13}C at 125 MHz), and chemical shifts are reported as δ (ppm) values relative to internal tetramethylsilane or the residual proton of the deuterated solvent. IR spectra were measured with a Perkin Elmer System 2000 FT-IR spectrometer. Mass spectra were recorded with a JEOL JMS-AX500 or JEOL JMS-SX102A spectrometer. Column chromatography was carried out with silica gel 60 (spherical, 70–140 mesh ASTM; Kanto Chemical Co., Japan).

2-[(Z)-2-Pentyl]-3-[tris(phenylthio)methyl]cyclopentanone (**5a** and **5b**). *n*-Butyllithium (0.40 ml, 0.67 mmol, as a 1.68 M hexane solution) was added dropwise to a solution of tris(phenylthio)methane (227 mg, 0.67 mmol) in dry THF (3 ml) over 5 min at -78°C under argon. The clear yellow solution was stirred for 20 min at -78°C, then a solution of **4** (100 mg, 0.67 mmol) in dry THF (2 ml) was added dropwise over 5 min. The reaction mixture was allowed to warm to r.t. over 60 min, then poured into sat. aq. NH_4Cl and extracted with EtOAc (30 ml × 3). The combined extracts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Purification of the residue by column chromatography (20 g of silica gel, hexane:AcOEt = 20:1) gave **5a** (*trans*-isomer, 168 mg, 0.34 mmol, 51%) as colorless needles and **5b** (*cis*-isomer, 90 mg, 0.18 mmol, 27%) as a yellow oil.

5a (*trans*-isomer): mp 92–93°C; IR ν_{max} (film) cm^{-1}: 2960, 1736, 1473, 1438, 748, 689; ^{1}H-NMR ($CDCl_3$) δ: 0.84 (3H, t, J=7.3 Hz, CH_2Me), 1.75–1.97 (3H, m), 2.10 (1H, m), 2.32–2.49 (4H, m), 2.69 (1H, m), 3.04 (1H, m), 5.06, 5.34 (each 1H, m, vinyl-H), 7.28–7.40 (9H, m), 7.59–7.70 (6H, m); ^{13}C-NMR ($CDCl_3$) δ: 14.0, 20.3, 23.4, 29.8, 37.7, 50.0, 51.4, 81.8, 123.8, 128.3, 129.1, 131.4, 134.4, 136.1, 220.6; EIMS *m/z*: 491 (M^++1), 381 (M^+−SPh); HRMS *m/z* (M^+−SPh): calcd. for $C_{23}H_{25}OS_2$, 381.1349; found, 381.1371.

5b (*cis*-isomer): IR ν_{max} (film) cm^{-1}: 2962, 1739, 1472, 1438, 750, 689; ^{1}H-NMR ($CDCl_3$) δ: 0.99 (3H, t, J=7.3 Hz, CH_2Me), 1.94 (1H, m), 2.08–2.13 (2H, m), 2.17–2.25 (1H, m), 2.27–2.45 (3H, m), 2.54 (1H, m), 2.68 (1H, m), 3.11 (1H, m), 5.39, 5.48 (each 1H, m, vinyl-H), 7.29–7.40 (9H, m), 7.43–7.64 (6H, m); ^{13}C-NMR ($CDCl_3$) δ: 14.1, 20.6, 23.4, 24.2, 36.3, 51.0, 51.9, 78.0, 125.2, 128.4, 129.3, 131.5, 133.2, 136.4, 216.9; EIMS *m/z*: 491 (M^+−1), 381 (M^+−SPh); HRMS *m/z* (M^+−SPh): calcd. for $C_{23}H_{25}OS_2$, 381.1349; found, 381.1308.

3-Ethoxycarbonyl-2-[(Z)-2-pentenyl]cyclopentanone (*OPC-1:0 ethyl ester*, **5c**). A mixture of **5a** (176 mg, 0.36 mmol), mercuric chloride (780 mg, 2.86 mmol), and mercuric oxide (309 mg, 1.43 mmol) in ethanol (8.0 ml) was stirred for 4 h at r.t. The reaction mixture was filtered through a Celite pad, and the filtrate was poured into water and extracted with ether (20 ml × 3). The combined extracts were successively washed with sat. aq. NH_4Cl and brine, dried over anhydrous Na_2SO_4, and concentrated under atomospheric pressure. The residue was purified by column chromatography (20 g of silica gel, pentane:ether = 10:1) to give **5c** (51 mg, 0.23 mmol, 63%) and by-product **5d** (6 mg, 0.03 mmol, 7%).

5c: IR ν_{max} (film) cm^{-1}: 2966, 2876, 1739, 1732, 1463, 1378, 1196, 1029, 862; ^{1}H-NMR ($CDCl_3$) δ: 0.95 (3H, t, J=7.3 Hz, CH_2Me), 1.28 (3H, t, J=7.3 Hz, CO_2CH_2Me), 1.92–2.61 (9H, m), 2.79 (1H, m), 4.18 (2H, q, J=7.3 Hz, CO_2CH_2Me), 5.20, 5.45 (each 1H, m, vinyl-H); ^{13}C-NMR ($CDCl_3$) δ: 13.8, 13.9, 20.2, 24.5, 25.6, 37.3, 45.7, 52.0, 60.6, 124.0, 134.3, 174.1, 217.1; EIMS *m/z*: 224 (M^+), 179 (M^+−OEt), 151 (M^+−$C_2H_4CO_2Et$); HRMS *m/z* (M^+): calcd. for $C_{13}H_{20}O_3$, 224.1413; found, 224.1441.

3-Ethoxycarbonyl-2-[(Z)-2-pentenyl]cyclopenten-1-one (**5d**). IR ν_{max} (film) cm^{-1}: 2965, 2875, 1716, 1447, 1374, 1187, 1029, 859; ^{1}H-NMR ($CDCl_3$) δ: 0.97 (3H, t, J=7.3 Hz, CH_2Me), 1.37 (3H, t, J=7.3 Hz, CO_2CH_2Me), 2.18 (2H, m), 2.46 (2H, m), 2.77 (2H, m), 3.32 (2H, d), 4.33 (2H, q, J=7.3 Hz, CO_2CH_2Me), 5.28, 5.41 (each 1H, m, vinyl-H); ^{13}C-NMR ($CDCl_3$) δ: 13.9, 14.0, 20.4, 22.3, 26.4, 33.8, 61.1, 123.6, 133.5, 149.1, 154.3, 165.1, 209.0; EIMS *m/z*: 222 (M^+), 193 (M^+−Et), 149

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($M^+ - CO_2Et$); HRMS *m/z* (M^+): calcd. for $C_{13}H_{18}O_3$, 222.1256; found, 222.1259.

{3-Oxo-2-[(2Z)-2-pentenyl]cyclopentyl}carboxylic acid (OPC-1:0, **5e**). To a solution of **5c** (92 mg, 0.41 mmol) in ethanol (0.4 ml) was added 3 N KOH (0.4 ml, 1.2 mmol). After stirring for 1.5 h, the reaction mixture was poured into water (10 ml), washed with ether (10 ml, 5 ml × 2), and acidified with 2 N HCl. The aqueous layer was extracted with ether (10 ml, 5 ml × 2), and the combined extracts were washed with water, dried over anhydrous Na_2SO_4, and concentrated under atmospheric pressure. The crude residue was purified by column chromatography (5 g of silica gel, pentane : ether : AcOH = 90 : 10 : 1) to give **5e** (65 mg, 81%) as a pale yellow oil; IR ν_{max} (film) cm^{-1}: 2965, 1732, 1715, 1456, 1435, 1157, 931 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 0.95 (3H, t, J = 7.3 Hz, $CH_2\underline{Me}$), 1.98–2.29 (4H, m), 2.33–2.60 (6H, m), 2.86 (1H, m), 5.21, 5.48 (each 1H, m, vinyl-H); ^{13}C-NMR ($CDCl_3$) δ: 13.9, 20.3, 24.5, 25.7, 37.3, 45.2, 51.7, 123.6, 134.8, 180.0, 216.9; EIMS *m/z*: 196 (35, M^+), 151 (40), 83 (100); HRMS *m/z* (M^+): calcd. for $C_{11}H_{16}O_3$, 196.1100; found, 196.1106.

Typical procedure for preparing iodo-esters **7a**–**7f**. A mixture of ethyl 3-bromopropionate (25 g, 0.138 mol) and sodium iodide (30 g, 200 mmol) in acetone (300 ml) was refluxed for 15 h under argon. The mixture was filtered, and the inorganic salts were washed with acetone. The combined filtrate and washings were concentrated under reduced pressure. The residue was diluted with ether (200 ml) and successively washed with 10% aq. $Na_2S_2O_3$ (200 ml), sat. aq. $NaHCO_3$ (200 ml), and brine (200 ml). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Distillation of the crude product *in vacuo* gave **7a** (27.5 g, 88%) as a pale yellow oil. The other iodo-esters were prepared by a similar procedure.

Ethyl 3-iodopropionate (**7a**). 27.5 g, 88%; bp 84–86°C (15 mmHg); ^{1}H-NMR ($CDCl_3$) δ: 1.28 (3H, t, J = 7.3 Hz, $CH_2\underline{Me}$), 3.00 (2H, t, J = 7.3 Hz, $\underline{CH_2}CO_2Et$), 3.33 (2H, t, J = 7.3 Hz, $\underline{CH_2}I$), 4.18 (2H, q, J = 7.3 Hz, $CO_2\underline{CH_2}Me$); EIMS *m/z*: 228 (M^+), 183 ($M^+ - OEt$), 101 ($M^+ - I$); HRMS *m/z* (M^+): calcd. for $C_5H_9O_2I$, 227.9606; found, 227.9611.

Ethyl 4-iodobutyrate (**7b**). 24.7 g, 57%; bp 58–60°C (1.0 mmHg); ^{1}H-NMR ($CDCl_3$) δ: 1.24 (3H, t, J = 7.3 Hz, $CH_2\underline{Me}$), 2.21 (2H, quint., J = 7.3 Hz, $\underline{CH_2}$), 2.42 (2H, t, J = 7.3 Hz, $\underline{CH_2}CO_2Et$), 3.17 (2H, t, J = 7.3 Hz, $\underline{CH_2}I$), 4.12 (2H, q, J = 7.3 Hz, $CO_2\underline{CH_2}Me$); EIMS *m/z*: 242 (M^+), 197 ($M^+ - OEt$), 115 ($M^+ - I$); HRMS *m/z* ($M^+ - OEt$): calcd. for C_4H_6OI, 196.9465; found, 196.9478.

Ethyl 5-iodopentanoate (**7c**). 30.6 g, 86%; bp 84–85°C (1.7 mmHg); ^{1}H-NMR ($CDCl_3$) δ: 1.24 (3H, t, J = 7.3 Hz, $CO_2CH_2\underline{Me}$), 1.68–1.93 (4H, m, 2 × $\underline{CH_2}$), 2.32 (2H, t, J = 7.3 Hz, $\underline{CH_2}CO_2Et$), 3.17 (2H, t, J = 7.3 Hz, $\underline{CH_2}I$), 4.12 (2H, q, J = 7.3 Hz, $CO_2\underline{CH_2}Me$); EIMS *m/z*: 257 ($M^+ + H$), 211 ($M^+ - OEt$), 129 ($M^+ - I$); HRMS *m/z* ($M^+ + H$): calcd. for $C_7H_{14}O_2I$, 257.0040; found, 257.0045.

Ethyl 6-iodohexanoate (**7d**). 28.7 g, 85%; bp 81–85°C (0.6 mmHg); ^{1}H-NMR ($CDCl_3$) δ: 1.24 (3H, t, J = 7.3 Hz, $CO_2CH_2\underline{Me}$), 1.38–1.71 (4H, m, 2 × $\underline{CH_2}$), 1.84 (2H, quint., J = 7.3 Hz, $\underline{CH_2}$), 2.30 (2H, t, J = 7.3 Hz, $\underline{CH_2}CO_2Et$), 3.17 (2H, t, J = 7.3 Hz, $\underline{CH_2}I$), 4.12 (2H, q, J = 7.3 Hz, $CO_2\underline{CH_2}Me$); EIMS *m/z*: 270 (M^+), 225 ($M^+ - OEt$), 143 ($M^+ - I$); HRMS *m/z* ($M^+ + H$): calcd. for $C_8H_{16}O_2I$, 271.0197; found, 271.0170.

Ethyl 7-iodoheptanate (**7e**). 32.9 g, 90%; bp 98–99°C (0.9 mmHg); ^{1}H-NMR ($CDCl_3$) δ: 1.24 (3H, t, J = 7.3 Hz, $CO_2CH_2\underline{Me}$), 1.23–1.41 (4H, m, 2 × $\underline{CH_2}$), 1.62, 1.81 (each 2H, quint., J = 7.3 Hz, 2 × $\underline{CH_2}$), 2.28 (2H, t, J = 7.3 Hz, $\underline{CH_2}CO_2Et$), 3.17 (2H, t, J = 7.3 Hz, $\underline{CH_2}I$), 4.12 (2H, q, J = 7.3 Hz, $CO_2\underline{CH_2}Me$); EIMS *m/z*: 285 ($M^+ + H$), 239 ($M^+ - OEt$), 157 ($M^+ - I$); HRMS *m/z* ($M^+ + H$): calcd. for $C_9H_{18}O_2I$, 285.0353; found, 285.0395.

Ethyl 8-iodooctanate (**7f**). 21.5 g, 92%; bp 102–105°C (0.4 mmHg); ^{1}H-NMR ($CDCl_3$) δ: 1.24 (3H, t, J = 7.3 Hz, $CO_2CH_2\underline{Me}$), 1.23–1.41 (6H, m, 3 × $\underline{CH_2}$), 1.61, 1.81 (each 2H, quint., J = 7.3 Hz, 2 × $\underline{CH_2}$), 2.28 (2H, t, J = 7.3 Hz, $\underline{CH_2}CO_2Et$), 3.17 (2H, t, J = 7.3 Hz, $\underline{CH_2}I$), 4.11 (2H, q, J = 7.3 Hz, $CO_2\underline{CH_2}Me$); EIMS *m/z*: 299 ($M^+ + H$), 253 ($M^+ - OEt$), 171 ($M^+ - I$); HRMS *m/z* ($M^+ + H$): calcd. for $C_{10}H_{20}O_2I$, 299.0510; found, 299.0511.

Typical procedure for 1,4-conjugate addition of zinc–copper reagents (**8a**–**8f**) *to 2-[(Z)-2-pentenyl]cyclopenten-1-one* (**4**). A suspension of activated zinc (4.7 g, 72 mmol) in dry THF (5 ml) containing 1,2-dibromoethane (0.2 ml, 2.5 mmol) was heated at 63°C for 3 min and then cooled to r.t. To the mixture was added chlorotrimethylsilane (0.3 ml, 2.4 mmol). After 15 min at r.t., a solution of **7a** (14.3 g, 63 mmol) in dry THF (20 ml) was slowly added at 30°C. After this addition had been completed, the reaction mixture was stirred overnight at 68°C. To the cooled (−14°C) suspension was rapidly added a mixture of CuCN (4.84 g, 54 mmol) and LiCl (4.80 g, 113 mmol) in dry THF (40 ml) to give a zinc–copper reagent (**8a**). To this solution at −78°C, a solution of **4** (1.86 g, 12.4 mmol) and chlorotrimethylsilane (6.8 ml, 54 mmol) in dry ether (13 ml) was added dropwise over 10 min. After stirring for 1 h at −78°C, the reaction mixture was allowed to warm to r.t. and stirred for 36 h more at r.t. The reaction mixture was then poured into aq. NH_4Cl and extracted with ether (200 ml × 3). The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was treated with 2 N HCl (5 ml) in EtOH (50 ml) at r.t. for 15 min in order to hydrolyze the remaining silyl enol ether. After a conventional work-up, the crude product was purified by column chromatography (180 g of silica gel, hexane : ether = 3 : 2) to give **9a** (2.59 g, 83%) as a colorless oil. The other compounds (**9b**–**9f**) were prepared by a similar procedure.

Ethyl 3-{3-oxo-2-[(Z)-2-pentenyl]cyclopentyl}propionate (OPC-3:0 ethyl ester, **9a**). 2.6 g, 83%; IR ν_{max} (film) cm^{-1}: 2964, 2875, 1739, 1732, 1457, 1373, 1183, 1032, 860; ^{1}H-NMR ($CDCl_3$) δ: 0.95 (3H, t, J = 7.3 Hz, $CH_2\underline{Me}$), 1.26 (3H, t, J = 7.3 Hz, $CO_2CH_2\underline{Me}$), 1.41 (1H, m), 1.59 (1H, m), 1.81–1.99 (2H, m), 2.02–2.19 (5H, m), 2.21–2.43 (5H, m), 4.14 (2H, q, J = 7.3 Hz, $CO_2\underline{CH_2}Me$), 5.22, 5.41 (each 1H, m, vinyl-H); ^{13}C-NMR ($CDCl_3$) δ: 13.9, 14.0, 20.4, 25.1, 26.5, 29.5, 31.9, 37.7, 40.4, 54.6, 60.2, 124.9, 133.6, 173.1, 219.6 (*trans*-isomer); ^{13}C-NMR ($CDCl_3$) δ: 13.9, 14.0, 20.4, 22.4, 23.3, 29.5, 32.4, 35.1, 38.2, 53.2, 60.2, 125.6, 133.0, 173.1, 219.6 (*cis*-isomer); EIMS *m/z*: 252 (M^+), 207 ($M^+ - OEt$), 151 ($M^+ - C_2H_4CO_2Et$); HRMS *m/z* (M^+): calcd. for $C_{15}H_{24}O_3$, 252.1725; found, 252.1738.

Ethyl 4-{3-oxo-2-[(Z)-2-pentenyl]cyclopentyl}butyrate (OPC-4:0 ethyl ester, **9b**). 2.7 g, 82%; IR ν_{max} (film) cm^{-1}: 2963, 2874, 1738, 1732, 1462, 1373, 1181, 1033, 861; ^{1}H-NMR ($CDCl_3$) δ: 0.95 (3H, t, J = 7.3 Hz, $CH_2\underline{Me}$), 1.26 (3H, t, J = 7.3 Hz, $CO_2CH_2\underline{Me}$), 1.41 (1H, m), 1.59–1.99 (5H, m), 2.02–2.19 (5H, m), 2.21–2.43 (5H, m), 4.14 (2H, q, J = 7.3 Hz, $CO_2\underline{CH_2}Me$), 5.22, 5.41 (each 1H, m, vinyl-H); ^{13}C-NMR ($CDCl_3$) δ: 14.0, 14.1, 20.4, 22.4, 25.2, 26.7, 34.0, 34.2, 37.8, 40.7, 54.7, 60.1, 125.1, 133.4, 173.3, 220.1 (*trans*-isomer); ^{13}C-NMR ($CDCl_3$) δ: 14.0, 14.1, 20.4, 22.9, 24.5, 25.5, 27.5, 34.1, 35.1, 38.4, 53.3, 60.1, 125.8, 132.9, 173.3, 220.1 (*cis*-isomer); EIMS *m/z*: 266 (M^+), 221 ($M^+ - OEt$), 151 ($M^+ - C_3H_6CO_2Et$); HRMS *m/z* (M^+): calcd. for $C_{16}H_{26}O_3$, 266.1882; found, 266.1870.

Ethyl 5-{3-oxo-2-[(Z)-2-pentenyl]cyclopentyl}pentanoate (OPC-5:0 ethyl ester, **9c**). 2.5 g, 71%; IR ν_{max} (film) cm^{-1}: 2962, 2873, 1739, 1733, 1463, 1373, 1163, 1033, 859; ^{1}H-NMR ($CDCl_3$) δ: 0.96 (3H, t, J = 7.3 Hz, $CH_2\underline{Me}$), 1.26 (3H, t, J = 7.3 Hz, $CO_2CH_2\underline{Me}$), 1.36–1.52 (4H, m), 1.61–1.66 (3H, m), 1.72–1.80 (2H, m), 1.98–2.12 (5H, m), 2.29–2.34 (4H, m), 4.14 (2H, q, J = 7.3 Hz, $CO_2\underline{CH_2}Me$), 5.26, 5.40 (each 1H, m, vinyl-H); ^{13}C-NMR ($CDCl_3$) δ: 13.9, 14.0, 20.3, 24.9, 25.2, 26.4, 26.8, 34.0, 34.1, 37.8, 40.7, 54.7, 60.0, 125.1, 133.3, 173.4, 220.3 (*trans*-isomer); ^{13}C-NMR ($CDCl_3$) δ: 13.9, 14.0, 20.4, 22.3, 24.5, 24.8, 26.9, 27.5, 35.0, 38.3, 53.4, 60.0, 125.8, 132.8, 173.4, 220.3 (*cis*-isomer, one ^{13}C-signal overlapped with that of the *trans*-isomer); EIMS *m/z*: 280 (M^+), 235 ($M^+ - OEt$), 151 ($M^+ - C_4H_8CO_2Et$); HRMS *m/z* (M^+): calcd. for $C_{17}H_{28}O_3$, 280.2038; found, 280.2038.

Ethyl 6-{3-oxo-2-[(Z)-2-pentenyl]cyclopentyl}hexanoate (OPC-6:0 ethyl ester, **9d**). 2.9 g, 80%; IR ν_{max} (film) cm^{-1}: 2964, 2860, 1739, 1732, 1464, 1373, 1180, 1034, 861; ^{1}H-NMR ($CDCl_3$) δ: 0.95 (3H, t, J = 7.3 Hz, $CH_2\underline{Me}$), 1.26 (3H, t, J = 7.3 Hz, $CO_2CH_2\underline{Me}$), 1.30–1.54 (6H, m), 1.59–1.64 (3H, m), 1.76–1.82 (2H, m), 1.99–2.19 (5H, m), 2.22–2.36 (4H, m), 4.13 (2H, q, J = 7.3 Hz, $CO_2\underline{CH_2}Me$), 5.24, 5.36 (each 1H, m, vinyl-H); ^{13}C-NMR ($CDCl_3$) δ: 13.9, 14.0, 20.3, 24.7, 25.2, 26.5, 26.8, 29.1, 34.0, 34.3, 37.8, 40.8, 54.8, 60.0, 125.2, 133.2, 173.5, 220.4 (*trans*-isomer); ^{13}C-NMR ($CDCl_3$) δ: 13.9, 14.0, 20.4, 22.3, 24.5, 24.6, 27.1, 27.7, 29.0, 34.3, 35.0, 38.4, 53.4, 60.0, 125.9, 132.7, 173.5, 220.4 (*cis*-isomer); EIMS *m/z*: 294 (M^+), 249 ($M^+ - OEt$), 151 ($M^+ - C_5H_{10}CO_2Et$); HRMS *m/z* (M^+): calcd. for $C_{18}H_{30}O_3$, 294.2195; found, 294.2190.

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Ethyl 7-{3-oxo-2-[(Z)-2-pentenyl]cyclopentyl}heptanoate (OPC-7:0 ethyl ester, **9e**). 3.0 g, 79%; IR ν_{max} (film) cm^{-1}: 2964, 2857, 1739, 1732, 1464, 1373, 1180, 1034, 861; ^{1}H-NMR ($CDCl_3$) δ: 0.95 (3H, t, J=7.3 Hz, CH_2Me), 1.25 (3H, t, J=7.3 Hz, CO_2CH_2Me), 1.32–1.38 (8H, m), 1.59–1.73 (3H, m), 1.75–1.81 (2H, m), 1.96–2.18 (5H, m), 2.21–2.35 (4H, m), 4.12 (2H, q, J=7.3 Hz, CO_2CH_2Me), 5.23, 5.41 (each 1H, m, vinyl-H); ^{13}C-NMR ($CDCl_3$) δ: 13.9, 14.0, 20.3, 24.7, 25.2, 26.7, 26.8, 28.8, 29.2, 34.1, 34.4, 37.8, 40.9, 54.8, 59.9, 125.2, 133.2, 173.6, 220.5 (*trans*-isomer); ^{13}C-NMR ($CDCl_3$) δ: 13.9, 14.0, 20.4, 22.3, 24.5, 26.6, 27.3, 27.8, 29.2, 34.1, 34.4, 35.0, 38.4, 53.4, 59.9, 125.9, 132.7, 173.6, 220.5 (*cis*-isomer); EIMS *m/z*: 308 (M^+), 263 ($M^+ - OEt$), 151 ($M^+ - C_6H_{12}CO_2Et$); HRMS *m/z* (M^+): calcd. for $C_{19}H_{32}O_3$, 308.2351; found, 308.2321.

Ethyl 8-{3-oxo-2-[(Z)-2-pentenyl]cyclopentyl}octanoate (OPC-8:0 ethyl ester, **9f**). 3.0 g, 74%; IR ν_{max} (film) cm^{-1}: 2930, 2856, 1739, 1732, 1464, 1373, 1179, 1035; ^{1}H-NMR ($CDCl_3$) δ: 0.95 (3H, t, J=7.3 Hz, CH_2Me), 1.24 (3H, t, J=7.3 Hz, CO_2CH_2Me), 1.31–1.38 (10H, m), 1.59–1.75 (3H, m), 1.77–1.81 (2H, m), 1.96–2.09 (5H, m), 2.20–2.36 (4H, m), 4.11 (2H, q, J=7.3 Hz, CO_2CH_2Me), 5.24, 5.41 (each 1H, m, vinyl-H); ^{13}C-NMR ($CDCl_3$) δ: 13.95, 14.04, 20.3, 24.7, 25.2, 26.8, 26.8, 28.9, 29.0, 29.4, 34.1, 34.5, 37.8, 40.9, 54.8, 59.9, 125.2, 133.2, 173.6, 220.5 (*trans*-isomer); ^{13}C-NMR ($CDCl_3$) δ: 13.95, 14.04, 20.4, 22.3, 24.6, 24.7, 27.4, 27.8, 28.8, 29.3, 31.2, 34.1, 35.1, 38.4, 53.5, 59.9, 125.9, 132.7, 173.6, 220.5 (*cis*-isomer): EIMS *m/z*: 322 (M^+), 277 ($M^+ - OEt$), 151 ($M^+ - C_7H_{14}CO_2Et$); HRMS *m/z* (M^+): calcd. for $C_{20}H_{34}O_3$, 322.2508; found, 322.2489.

Typical procedure for alkaline hydrolysis of esters **9a**–**9f**. To a solution of **9a** (351 mg, 1.39 mmol) in ethanol (1.4 ml) was added 3 N KOH (1.4 ml, 4.2 mmol). After stirring for 3 h, the reaction mixture was poured into water (30 ml), washed with ether (30 ml, 20 ml × 2), and acidified with 2 N HCl. The aqueous layer was extracted with ether (30 ml, 20 ml × 2), and the combined extracts were washed with water, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude residue was purified by column chromatography (20 g of silica gel, hexane:ether:AcOH = 75:25:1) to give **10a** (261 mg, 83%) as a pale yellow oil. The other compounds (**10b**–**10f**) were prepared by a similar procedure.

3-{3-Oxo-2-[(Z)-2-pentenyl]cyclopentyl}pentanoic acid (OPC-3:0, **10a**). 261 mg, 83%; IR ν_{max} (film) cm^{-1}: 2962, 1732, 1715, 1456, 1417, 1168, 921 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 0.95 (3H, t, J=7.3 Hz, CH_2Me), 1.25–1.48 (2H, m), 1.60–1.82 (5H, m), 1.99–2.17 (5H, m), 2.30–2.41 (4H, m), 5.25, 5.43 (each 1H, m, vinyl-H); ^{13}C-NMR ($CDCl_3$) δ: 13.9, 20.3, 25.1, 26.4, 29.2, 31.5, 37.6, 40.3, 54.6, 124.8, 133.6, 179.0, 220.0; EIMS *m/z*: 224 (34, M^+), 156 (32, $M^+ - C_5H_7$), 151 (88), 83 (100); HRMS *m/z* (M^+): calcd. for $C_{13}H_{20}O_3$, 224.1412; found, 224.1376.

4-{3-Oxo-2-[(Z)-2-pentenyl]cyclopentyl}butyric acid (OPC-4:0, **10b**). 429 mg, 93%; IR ν_{max} (film) cm^{-1}: 2930, 1733, 1710, 1456, 1410, 1164, 941 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 0.95 (3H, t, J=7.3 Hz, CH_2Me), 1.25–1.48 (2H, m), 1.60–1.82 (5H, m), 1.99–2.17 (5H, m), 2.30–2.41 (4H, m), 5.25, 5.43 (each 1H, m, vinyl-H); ^{13}C-NMR ($CDCl_3$) δ: 13.9, 20.3, 22.0, 25.2, 26.7, 33.8, 37.7, 40.7, 54.6, 125.0, 133.5, 179.0, 220.1; EIMS *m/z*: (238 (22, M^+), 170 (23), 151 (75), 83 (100); HRMS *m/z* (M^+): calcd. for $C_{14}H_{22}O_3$, 238.1569; found, 238.1546.

5-{3-Oxo-2-[(Z)-2-pentenyl]cyclopentyl}pentanoic acid (OPC-5:0, **10c**). 63 mg, 76%; IR ν_{max} (film) cm^{-1}: 2934, 1734, 1715, 1463, 1408, 1164, 977 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 0.96 (3H, t, J=7.3 Hz, CH_2Me), 1.25–1.46 (4H, m), 1.64–1.69 (3H, m), 1.74–1.85 (2H, m), 1.98–2.19 (5H, m), 2.29–2.39 (4H, m), 5.25, 5.43 (each 1H, m, vinyl-H); ^{13}C-NMR ($CDCl_3$) δ: 13.9, 20.3, 24.6, 25.2, 26.3, 26.8, 33.7, 34.1, 37.7, 40.7, 54.7, 125.1, 133.3, 179.3, 220.4; EIMS *m/z*: 252 (12, M^+), 234 (16), 184 (14), 151 (47), 82 (100); HRMS *m/z* (M^+): calcd. for $C_{15}H_{24}O_3$, 252.1714; found, 252.1725.

6-{3-Oxo-2-[(Z)-2-pentenyl]cyclopentyl}hexanoic acid (OPC-6:0, **10d**). 351 mg, 87%; IR ν_{max} (film) cm^{-1}: 2933, 1732, 1716, 1457, 1409, 1163, 940 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 0.96 (3H, t, J=7.3 Hz, CH_2Me), 1.25–1.46 (6H, m), 1.64–1.69 (3H, m), 1.74–1.85 (2H, m), 1.98–2.19 (5H, m), 2.29–2.39 (4H, m), 5.25, 5.43 (each 1H, m, vinyl-H); ^{13}C-NMR ($CDCl_3$) δ: 13.9, 20.3, 24.4, 25.2, 26.5, 26.8, 29.0, 33.7, 34.3, 37.8, 40.8, 54.8, 125.2, 133.3, 179.5, 220.6; EIMS *m/z*: 266 (6, M^+), 198 (21), 151 (42), 83 (100); HRMS *m/z* (M^+): calcd. for $C_{16}H_{26}O_6$, 266.1882; found, 266.1869.

7-{3-Oxo-2-[(Z)-2-pentenyl]cyclopentyl}heptanoic acid (OPC-7:0, **10e**). 438 mg, 93%; IR ν_{max} (film) cm^{-1}: 2931, 1739, 1710, 1463, 1408, 1161, 943 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 0.96 (3H, t, J=7.3 Hz, CH_2Me), 1.25–1.46 (8H, m), 1.64–1.69 (3H, m), 1.74–1.85 (2H, m), 1.98–2.19 (5H, m), 2.29–2.39 (4H, m), 5.25, 5.43 (each 1H, m, vinyl-H); ^{13}C-NMR ($CDCl_3$) δ: 13.9, 20.3, 24.4, 25.2, 26.6, 26.8, 28.8, 29.2, 33.7, 34.4, 37.8, 40.9, 54.8, 125.2, 133.2, 179.5, 220.7; EIMS *m/z*: 280 (4, M^+), 262 (8), 212 (17), 151 (42), 83 (100); HRMS *m/z* (M^+): calcd. for $C_{17}H_{28}O_3$, 280.2046; found, 280.2038.

8-{3-Oxo-2-[(Z)-2-pentenyl]cyclopentyl}octanoic acid (OPC-8:0, **10f**). 390 mg, 97%; IR ν_{max} (film) cm^{-1}: 2930, 1739, 1710, 1463, 1409, 1161, 942 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 0.96 (3H, t, J=7.3 Hz, CH_2Me), 1.25–1.33 (10H, m), 1.64–1.69 (3H, m), 1.74–1.85 (2H, m), 1.98–2.19 (5H, m), 2.29–2.39 (4H, m), 5.25, 5.43 (each 1H, m, vinyl-H); ^{13}C-NMR ($CDCl_3$) δ: 14.0, 20.3, 24.4, 25.2, 26.76, 26.81, 28.8, 29.0, 29.4, 33.8, 34.4, 37.8, 40.9, 54.8, 125.2, 133.2, 179.6, 220.8; EIMS *m/z*: 294 (4, M^+), 226 (20), 151 (48), 83 (100); HRMS *m/z* (M^+): calcd. for $C_{18}H_{30}O_3$, 294.2195; found, 294.2185.

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