Supporting Information for

Iodocarbocyclization Reaction of β -Ketoesters and alkynes

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Experimental procedures and spectral and analytical data for all products.

General Information. Unless otherwise noted all commercial materials were used without purification. TLC was performed on aluminum-backed plates coated with silica gel 60 with F₂₅₄ indicator (Scharlau). Flash column chromatography was carried out on silica gel 60, 230-240 mesh. ¹H NMR (300, 400 MHz) and ¹³C NMR (75.5, 100 MHz) spectra were measured at room temperature on AV-300 and AMX-400 instruments, respectively, and referenced to CDCl₃. Carbon multiplicities were assigned by DEPT techniques. High-resolution mass spectra (HRMS) were determined on a Finnigan MAT 95 spectrometer. Elemental analyses were carried out on a Perkin-Elmer 2400 and Carlo Erba 1108 microanalyzers.

Starting Materials:

Substrates **1a**, **1b**, **1c**, **1d**, **1h** were prepared by the alkylation method described by Malacria (method A).¹ Substrate **1j** was prepared by TiCl₄ mediated conjugate addition of triphenylallenylstannane (method B).²

Method A

Method B

¹ P. Cruciani, R. Stammer, C. Aubert, M. Malacria, *J. Org. Chem.* **1996**, 61, 2699.

² J. Haruta, K. Nishi, S. Matsuda, S. Akai, Y. Tamura, Y. Kita, *J. Org. Chem.* **1990**, 55, 4853.

Representative Procedure for Method A. Synthesis of 2-acetylhept-5-ynoic acid ethyl ester (1a). To a suspension of NaH (95 wt. %, 164 mg, 6.5 mmol, 1 equiv) in 8 mL of a 1:1 mixture of THF:DMF was added potassium iodide (600 mg, 3.6 mmol, 0.55 equiv). The solution was cooled to 0°C and treated dropwise with 3-oxo-butiric acid ethyl ester (928 mg, 7.14 mmol, 1.09 equiv). The resulting yellow solution was warmed to RT, stirred for 30 min then treated with methanesulfonic acid pent-3-ynyl ester³ (1.17g, 6.1 mmol, 0.93 equiv). The whole was heated to 95°C overnight, quenched with 5 mL of 1N HCl, and extracted with ether (3 x 10 mL). The combined organics were washed with brine (2 x 10 mL), dried over Mg SO₄, concentrated and purified by flash chromatography (hexanes:EtOAc, 7:1) to yield **1a** as a colorless oil (510 mg, 40 %). Data for the keto tautomer: ¹H NMR (300 MHz, CDCl₃) δ 4.19 (q, *J* = 7.2, 2H), 3.69 (t, *J* = 7.5, 1H), 2.27 (s, 3H), 2.19-2.16 (m, 2H), 2.1-1.97 (m, 2H), 1.77 (t, *J* = 2.4, 3H), 1.28 (t, *J* = 7.2, 3H). ¹³C NMR (75.5 MHz, CDCl₃) δ 202.7 (C), 169.26 (C), 77.2 (C), 77.1 (C), 61.25 (CH₂), 58.1 (CH), 29.1 (CH₃), 27.2 (CH₂), 16.7 (CH₂), 13.7 (CH₃), 3.6 (CH₃). IR ν(Neat, cm⁻¹): 1737, 1715. HRMS (EI): calcd for C₁₁H₁₆O₃: 196.1099; found: 196.1094.

2-benzoylhept-5-ynoic acid ethyl ester (1c). Yellow oil. *R*_f = 0.43 (Hexane: EtOAc, 10:1). ¹H NMR (300 MHz, CDCl₃) δ 8.03 (d, *J* = 7.2, 2H), 7.58 (t, *J* = 7.4, 1H), 7.48 (t, *J* = 7.1, 2H), 4.59 (t, *J* = 6.5, 1H), 4.15 (q, *J* = 7.2, 2H), 2.28-2.22 (m, 2H), 2.20-2.13 (m, 2H), 1.76 (t, *J* = 2.4, 3H), 1.17 (t, *J* = 7.2, 3H).

¹³C NMR (75.5 MHz, CDCl₃) δ 195.2 (C), 169.7 (C), 136.1 (C), 133.5 (CH), 128.7 (CH), 77.6 (C), 77.2 (C), 61.3 (CH₂), 52.5 (CH), 28.0 (CH₂), 16.9 (CH₂), 13.9 (CH₃), 3.3 (CH₃). IR ν(Neat, cm⁻¹): 1737, 1687. HRMS (EI): calcd for C₁₆H₁₈O₃: 258.1250; found: 258.1254.

2-Acetylhept-5-ynoic acid benzyl ester (1b). Colorless oil. *R*_f = 0.42 (Hexane: EtOAc, 7:1). ¹H NMR (300 MHz, CDCl₃) δ 7.42-7.34 (m, 5H), 5.19 (s, 2H), 3.77 (t, *J* = 7.0, 1H), 2.24 (s, 3H), 2.28-2.17 (m, 2H), 2.10-2.01 (m, 2H), 1.78 (t, *J* = 2.6, 3H).

¹³C NMR (75.5 MHz, CDCl₃) δ 202.5 (C), 169.2 (C), 135.2 (C), 128.5 (CH), 128.3 (CH), 128.1 (CH), 77.2 (C), 77.1 (C), 67.0 (CH₂), 58.0 (CH), 29.1 (CH₃), 26.9 (CH₂), 16.5 (CH₂), 3.3 (CH₃). IR ν(Neat, cm⁻¹): 1737, 1715. HRMS (FAB+, M⁺+1): calcd for C₁₆H₁₈O₃: 259.1334; found: 259.1336.

2-Acetyloct-5-ynoic acid ethyl ester (1d). Colorless oil. *R*_f = 0.36 (Hexane: EtOAc, 7:1). ¹H NMR (300 MHz, CDCl₃) δ 4.19 (q, *J* = 7.2, 2H), 3.66 (t, *J* = 7.2, 1H), 2.27 (s, 3H), 2.23-2.13 (m, 4H), 2.10-2.01 (m, 2H), 1.28 (t, *J* = 6.9, 3H), 1.11 (t, *J* = 7.5, 3H).

¹³C NMR (75.5 MHz, CDCl₃) δ 202.9 (C), 169.4 (C), 83.3 (C), 77.4 (C), 61.4 (CH₂), 58.1 (CH), 29.3 (CH₃), 27.1 (CH₂), 16.7 (CH₂), 14.2 (CH₂), 14.1 (CH₃), 12.3 (CH₃). IR ν(Neat, cm⁻¹): 1737, 1715. HRMS (FAB+, M⁺+1): calcd for C₁₂H₁₈O₃: 211.1334; found: 211.1333.

³ A. T. Hewson D.T.; MacPherson, *J. Chem. Soc., Perkin Trans. 1*, **1985**, 12, 2625

3-(pent-3-ynyl)pentane-2,4-dione (1h). Colorless oil. R_f = 0.37 (Hexane: EtOAc, 5:1). Data for the mixture keto-enol: ^1H NMR (300 MHz, CDCl_3) δ 3.85 (t, J = 6.9, 1H), 2.43 (t, J = 7.8, 1H), 2.18 (s, 3H), 2.14 (s, 3H), 2.16-2.09 (m, 1H), 2.00-1.93 (m, 2H), 1.73 (t, J = 1.5, 3H).

^{13}C NMR (75.5 MHz, CDCl_3) δ 203.9 (C), 191.5 (C), 109.1 (C), 77.9 (C), 77.4 (C), 77.1 (C), 76.7 (C), 67.1 (CH), 29.4 (CH_3), 27.1 (CH_2), 26.9 (CH_2), 19.9 (CH_2), 16.9 (CH_2), 3.34 (CH_3). IR ν (Neat, cm^{-1}): 1727, 1698. HRMS (EI): calcd for $\text{C}_{10}\text{H}_{14}\text{O}_2$: 166.0988; found: 166.0987.

Method B. Synthesis of 2-oxo-6-(prop-2-ynyl)cyclohexanecarboxylic acid Ethyl ester (1j).⁴ To a cold (-78°C) solution of 2-(ethoxycarbonyl)-2-cyclohexenone (384mg, 2.3 mmol, 1 equiv) in 4 mL dichloromethane was added TiCl_4 dropwise (1M in dichloromethane, 3.0 mL, 3.0 mmol, 1.3 equiv). After 10 min a solution of triphenylallenyl tin (1.85 g, 4.6 mmol, 2 equiv) in 4 mL in dichloromethane **was added**. The resulting solution was allowed to gradually reach RT over 2 hours and stirred overnight. The reaction was quenched with 10 mL water and extracted with EtOAc (3 x 10 mL). The combined extracts were dried over Na_2SO_4 concentrated, taken up in 20 mL of diethyl ether, and treated with 10 mL of saturated KF. The resulting suspension was stirred at RT for 1 hour, filtered, and extracted with Ethyl acetate (3 x 10 mL). The combined extracts were dried over Na_2SO_4 , and concentrated to yield a crude oil which was purified by flash chromatography (hexanes: ether, 3:1) to yield a colorless oil (276 mg, 58%). Data for the keto-enol mixture: ^1H NMR (400 MHz, CDCl_3) δ 12.47 (s, 1H), 4.22 (m, 2H), 2.91-2.78 (m, 1H), 2.55-1.95 (m, 6H), 1.82-1.63 (m, 2H), 1.60-1.53 (m, 1H), 1.28 (t, J = 3.2, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 206.3 (C), 173.9 (C), 172.4 (C), 100.8 (C), 79.4 (C), 69.0 (C), 61.3 (CH_2), 60.4 (CH_2), 41.3 (CH_2), 39.8 (CH), 31.4 (CH), 29.3 (CH_2), 29.1 (CH_2), 25.7 (CH_2), 25.4 (CH_2), 23.5 (CH_2), 23.1 (CH_2), 22.5 (CH_2), 17.0 (CH_2), 14.3 (CH_3).

Eliminado: was added.

Eliminado:

Substrates **1f**, **1g** and **1i** were prepared by iodination or bromination of the corresponding terminal alkynes as described by Denmark.⁵

2-acetyl-6-bromohex-5-ynoic acid ethyl ester (1f). Yellow oil. R_f = 0.28 (Hexane: EtOAc, 7:1). ^1H NMR (300 MHz, CDCl_3) δ 4.21 (q, J = 7.8, 2H), 3.65 (t, J = 7.5, 1H), 2.27 (s, 3H), 2.31-2.25 (m, 2H), 2.08-2.02 (m, 2H), 1.28 (t, J = 6.9, 3H).

^{13}C NMR (75.5 MHz, CDCl_3) δ 202.5 (C), 169.2 (C), 78.5 (C), 61.6 (CH_2), 58.0 (CH), 39.7 (C), 29.5 (CH_3), 26.3 (CH_2), 17.6 (CH_2), 13.8 (CH_3). IR ν (Neat, cm^{-1}): 1732, 1715. HRMS (FAB+, $\text{M}^+ + 1$): calcd for $\text{C}_{10}\text{H}_{13}\text{O}_3\text{Br}$: 261.0126; found: 261.0136.

⁴ Product described in this reference: Steven t. Staben, Joshua J. Kennedy-Smith and F. Dean Toste, *Angew. Chem. Int. Ed.* **2004**, 43, 5350-5352.

⁵ S. E. Denmark, S.-M. Yang, *J. Am. Chem. Soc.* **2002**, 124, 15196.

2-acetyl-6-iodohex-5-ynoic acid ethyl ester (1g). Yellow oil. R_f = 0.24 (Hexane: EtOAc, 7:1). ^1H NMR (300 MHz, CDCl_3) δ 4.20 (q, J = 7.1, 2H), 3.64 (t, J = 7.1, 1H), 2.42 (t, J = 6.8, 2H), 2.27 (s, 3H), 2.08-2.00 (m, 2H), 1.28 (t, J = 7.2, 3H).

^{13}C NMR (75.5 MHz, CDCl_3) δ 202.5 (C), 169.2 (C), 92.7 (C), 61.6 (CH_2), 57.9 (CH), 29.4 (CH_3), 26.4 (CH_2), 18.6 (CH_2), 14.1 (CH_3), -4.9 (C). IR v(Neat, cm^{-1}): 1737, 1712. HRMS (EI): calcd for $\text{C}_{10}\text{H}_{13}\text{O}_3\text{I}$: 307.9904; found: 307.9905.

2-oxo-6-(3-iodoprop-2-ynyl)cyclohexanecarboxylic acid ethyl ester (1l). Yellow oil. R_f = 0.29 (Hexane: EtOAc, 7:1). Data for the keto-enol mixture: ^1H NMR (400 MHz, CDCl_3) δ 12.47 (s, 1H), 4.22 (m, 2H), 2.52-2.23 (m, 5H), 2.15-1.95 (m, 2H), 1.88-1.63 (m, 2H), 1.28 (t, J = 3.2, 3H).

^{13}C NMR (100 MHz, CDCl_3) δ 206.3 (C), 173.9 (C), 172.3 (C), 170.4 (C), 93.8 (C), 90.2 (C), 84.6 (C), 80.4 (C), 61.6 (CH_2), 61.3 (CH_2), 60.3 (CH_2), 40.9 (CH_2), 39.6 (CH), 31.6 (CH), 29.2 (CH_2), 29.1 (CH_2), 25.9 (CH_2), 25.8 (CH_2), 24.6 (CH_2), 23.7 (CH_2), 16.9 (CH_2), 14.2 (CH_3),.. IR v(Neat, cm^{-1}): 1740, 1712, 1643, 1610. HRMS (EI): calcd for $\text{C}_{10}\text{H}_{13}\text{O}_3\text{I}$: 334.0066; found: 334.0065.

Substrates **1e** and **1k** were prepared by Sonogashira coupling reactions of iodobenzene with the corresponding terminal alkynes (method C).

Method C

Representative Procedure for Method C. Synthesis of 2-oxo-6-(3-phenylprop-2-ynyl)cyclohexanecarboxylic acid ethyl ester (1k). To a solution of 2-oxo-6-(prop-2-ynyl)cyclohexanecarboxylic acid Ethyl ester **1j** (193 mg, 0.93 mmol, 1.1 equiv), iodobenzene (175 mg, 0.84 mmol, 1 equiv) in Et_3N (2 mL) was added $\text{PdCl}_2(\text{PPh}_3)_2$ (32 mg, 0.05 mmol, 0.05 equiv). After 10 min, was added CuI (9 mg, 0.05 mmol, 0.05 equiv). The resulting heterogeneous mixture was stirred for 1h and then was diluted with diethyl ether (10 ml). The organic layer is separated, filtered through a short pad of zelite and evaporated. Chromatographic purification of the crude product (hexanes/ethyl acetate, 7/1) affords the ketoester **1k** as a yellow oil (147m g, 62%). Data for the keto-enol mixture: ^1H NMR (400 MHz, CDCl_3) δ 12.54 (s, 1H), 7.41-7.38 (m, 2H), 7.29-7.27 (m, 3H), 4.28-4.25 (m, 2H), 2.87-2.86 (m, 1H), 2.73 (d, J = 4.8, 1H), 2.54-2.48 (m, 1H), 2.43-2.39 (m, 1H), 2.36-2.3 (m, 1H), 2.29-2.01 (m, 1H), 1.93-1.61 (m, 3H), 1.31 (t, J = 3.2, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 205.9 (C), 173.7 (C), 172.2 (C), 169.8 (C), 131.3 (CH), 128.0 (CH), 127.9 (CH), 127.6 (CH), 123.8 (C), 100.6 (C), 89.1 (C), 85.3 (C), 82.6 (C), 81.4 (C), 60.4 (CH), 60.3 (CH_2), 60.2 (CH_2), 40.2 (CH_2), 39.7 (CH), 31.6 (CH), 29.1 (CH_2), 25.8 (CH_2), 24.3 (CH_2), 16.9 (CH_2), 14.2 (CH_3). IR v(Neat, cm^{-1}): 1741, 1713, 1644, 1611. HRMS (EI): calcd for $\text{C}_{18}\text{H}_{20}\text{O}_3$: 284.1407; found: 284.1404.

2-acetyl-6-phenylhex-5-ynoic acid ethyl ester (1e). Yellow oil. $R_f = 0.33$ (Hexane: EtOAc, 7:1). ^1H NMR (300 MHz, CDCl_3) δ 7.43-7.33 (m, 2H), 7.32-7.21 (m, 3H), 4.22 (q, $J = 7.0$, 2H), 3.75 (t, $J = 6.8$, 1H), 2.53-2.40 (m, 2H), 2.31 (s, 3H), 2.20-2.08 (m, 2H), 1.29 (t, $J = 7.2$, 3H).

^{13}C NMR (75.5 MHz, CDCl_3) δ 202.2 (C), 169.9 (C), 143.2 (C), 131.5 (CH), 128.2 (CH), 127.9 (CH), 88.1 (C), 82.0 (C), 61.5 (CH_2), 58.2 (CH), 29.5 (CH_3), 26.7 (CH_2), 17.4 (CH_2), 14.1 (CH_3). IR v(Neat, cm^{-1}): 1737, 1713. HRMS (EI): calcd for $\text{C}_{16}\text{H}_{18}\text{O}_3$: 258.1250; found: 258.1254.

Substrate **1i** was prepared by a sequence similar to that described by Wulff.⁶

Synthesis of 5-(hex-1-ynyl)-5-methoxy-2-oxocyclohexanecarboxylic acid ethyl ester (**1i**).

To a cold solution (-78°C) of 1-hexyne (0.83 g, 10 mmol, 1 equiv) in 15 mL of THF was added BuLi dropwise (1.6 M in hexanes, 7.5 mL, 12 mmol, 1.2 equiv). After 1h a solution of cyclohexanone **A** (1.57g, 10 mmol, 1 equiv) in 5 mL of THF. The mixture was stirred at -78°C for 2h, warmed at RT and then quenched with 15 mL of HCl (aq) 1N. Extraction with Et_2O (3 x 15 mL), drying (MgSO_4) and evaporation gave the alkynol **B** as a yellow oil (2.26 g, 95 %) used in the next step without purification. ^1H NMR (400 MHz, CDCl_3) δ 3.91 (s, 4H), 2.18 (t, $J = 6.9$, 2H), 1.93-1.83 (m, 4H), 1.75 (t, $J = 6.0$, 4H), 1.49-1.34 (m, 4H), 0.88 (t, $J = 7.16$, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 108.1 (C), 84.6 (C), 83.1 (C), 67.4 (C), 64.3 (CH_2), 37.5 (CH_2), 31.6 (CH_2), 30.8 (CH_2), 21.9 (CH_2), 18.3 (CH_2), 13.5 (CH_3).

To a cold solution (0°C) of alkynol **B** (2.26 g, 9.5 mmol, 1 equiv) in 15 mL of DMF was added slowly NaH (95 wt. %, 0.97 g, 12 mmol, 1.3 equiv). After 30 min was added MeI (0.73 mL, 11.7 mmol, 1.2 equiv). The mixture was allowed to warm to RT and stirred for 24 h. The reaction was quenched with 15 mL of water and extracted with Et_2O (2 x 20 mL). The organic layer was washed with brine (2 x 20 mL), dried over MgSO_4 and concentrated to give a yellow oil which was treated with conc. HCl (2 mL), acetone (11mL) and H_2O (16 mL). After the mixture was stirred for 27 h, it was neutralized with solid K_2CO_3 , extracted with a large excess of Et_2O , dried over MgSO_4 and purified by flash chromatography (hexanes: AcOEt, 3:1) to yield ketone **C** as a yellow oil (1.24 g, 60%). ^1H NMR (300 MHz, CDCl_3) δ 3.43 (s, 3H), 2.51-2.32 (m, 4H), 2.23 (t, $J = 7.1$, 2H), 2.12 (t, $J = 6.7$, 4H), 1.53-1.36 (m, 4H), 0.91 (t, $J = 7.2$, 3H).

⁶ W. D. Wulff, J. Su, P.-C. Tang, X. Yao-Chang, *Synthesis* **1999**, 3, 415

^{13}C NMR (75.5 MHz, CDCl_3) δ 210.5 (C), 87.3 (C), 78.9 (C), 71.5 (C), 51.2 (CH_3), 37.4 (CH_2), 35.8 (CH_2), 30.6 (CH_2), 21.8 (CH_2), 18.1 (CH_2), 13.4 (CH_3).

To a cold (0°C) suspension of NaH (95 wt. %, 288 mg, 11.4 mmol, 3.1 equiv) in 6 mL of diethyl carbonate was added a solution of ketone **C** (769 mg, 3.68 mmol, 1 equiv) in 4 mL of diethyl carbonate. The resulting mixture was warmed to RT and stirred for 89 h. The reaction was quenched with 8 mL of 1N HCl and extracted with ether (3 x 10 mL). The combined organics were washed with brine (2 x 10 mL), dried over Mg SO_4 , concentrated and purified by flash chromatography (hexanes:EtOAc, 7:1) to yield **1i** as a yellow oil (453 mg, 44 %). Data for the enol tautomer: ^1H NMR (400 MHz, CDCl_3) δ 12.26 (s, 1H), 4.20 (q, $J = 7.0$, 2H), 3.37 (s, 3H), 2.63-2.50 (m, 2H), 2.40 (t, $J = 6.5$, 2H), 2.21 (t, $J = 6.9$, 2H), 1.95 (t, $J = 6.0$, 2H), 1.51-1.39 (m, 4H), 1.29 (t, $J = 7.1$, 3H), 0.91 (t, $J = 7.1$, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 172.1 (C), 171.1 (C), 94.1 (C), 85.9 (C), 79.7 (C), 71.1 (C), 60.2 (CH_2), 50.9 (CH_3), 34.2 (CH_2), 31.4 (CH_2), 30.6 (CH_2), 26.4 (CH_2), 21.7 (CH_2), 18.1 (CH_2), 14.1 (CH_3), 13.4 (CH_3). IR ν (Neat, cm^{-1}): 1742, 1658. HRMS (EI): calcd for $\text{C}_{16}\text{H}_{24}\text{O}_4$: 280.1669; found: 280.1673.

General procedure for Iodocarbocyclization Reaction. Synthesis of 1-acetyl-3-iodo-2-methylcyclopent-2-enecarboxylic acid ethyl ester (2a). To a solution of ketoester **1a** (196 mg, 1 mmol, 1 equiv) in 20 mL of CH_2Cl_2 was added I_2 (254 mg, 1 mmol, 1 equiv). The resulting mixture was stirred at RT for 5 h, concentrated and purified by flash chromatography (hexanes:EtOAc, 7:1) to yield **2a** as a yellow oil (225 mg, 70 %). ^1H NMR (400 MHz, CDCl_3) δ 4.20 (q, $J = 7.2$, 2H), 2.88-2.61 (m, 3H), 2.28-2.18 (m, 1H), 2.16 (s, 3H), 1.88 (t, $J = 2.4$, 3H), 1.28 (t, $J = 7.1$, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 203.8 (C), 170.7 (C), 141.1 (C), 100.1 (C), 73.5 (C), 62.0 (CH_2), 42.5 (CH_2), 33.0 (CH_2), 27.0 (CH_3), 18.1 (CH_3), 14.5 (CH_3). IR ν (Neat, cm^{-1}): 1732, 1712. HRMS (FAB+, $\text{M}^+ + 1$): calcd for $\text{C}_{11}\text{H}_{15}\text{IO}_3$: 323.0144; found: 323.0140, Elemental analysis (%) calcd: C 41.01, H 4.69; found: C 40.85, H 4.62.

1-benzoyl-3-iodo-2-methylcyclopent-2-enecarboxylic acid ethyl ester (2c). Yellow oil. $R_f = 0.68$ (Hexane: CH_2Cl_2 , 1:1). ^1H NMR (400 MHz, CDCl_3) δ 7.67 (d, $J = 6.6$, 2H), 7.56-7.51 (m, 1H), 7.42 (t, $J = 7.4$, 2H), 4.11 (q, $J = 7.1$, 2H), 3.16-3.07 (m, 1H), 2.96-2.85 (m, 1H), 2.77-2.66 (m, 1H), 2.33-2.23 (m, 1H), 1.90 (t, $J = 2.6$, 3H), 1.04 (t, $J = 7.1$, 3H).

^{13}C NMR (100 MHz, CDCl_3) δ 195.7 (C), 170.9 (C), 141.0 (C), 134.9 (C), 132.9 (CH), 128.6 (CH), 128.5 (CH), 99.1 (C), 70.9 (C), 61.8 (CH_2), 42.5 (CH_2), 33.9 (CH_2), 17.7 (CH_3), 13.9 (CH_3). IR ν (Neat, cm^{-1}): 1716, 1687. HRMS (EI): calcd for $\text{C}_{16}\text{H}_{17}\text{IO}_3$: 384.0222; found: 384.0229.

1-Acetyl-3-iodo-2-methylcyclopent-2-enecarboxylic acid benzyl ester (2b). Yellow oil. $R_f = 0.50$ (Hexane: AcOEt, 7:1). ^1H NMR (400 MHz, CDCl_3) δ 7.40-7.30 (m, 5H), 5.25-5.14 (AB system, $J = 6.8$, 2H), 2.86-2.63 (m, 3H), 2.29-2.21 (m, 1H), 2.11 (s, 3H), 1.90 (t, $J = 2.6$, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 203.5 (C), 170.5 (C), 141.0 (C), 135.6 (C), 129.1 (CH), 128.9 (CH), 128.7 (CH), 100.4 (C), 73.6 (C), 67.8 (CH_2), 42.6 (CH_2), 33.1

(CH₂), 27.0 (CH₃), 18.1 (CH₃). IR ν (Neat, cm⁻¹): 1737, 1712. HRMS (EI): calcd for C₁₆H₁₇IO₃: 384.0222; found: 384.0235.

1-Acetyl-2-ethyl-3-iodocyclopent-2-enecarboxylic acid ethyl ester (2d). Light yellow oil. R_f = 0.36 (Hexane: AcOEt, 7:1). ¹H NMR (400 MHz, CDCl₃) δ 4.30-4.13 (m, 2H), 2.82-2.62 (m, 3H), 2.37-2.19 (m, 3H), 2.16 (s, 3H), 1.28 (t, J = 7.0, 3H), 0.98 (t, J = 7.1, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 203.6 (C), 170.7 (C), 145.7 (C), 99.2 (C), 72.9 (C), 61.7 (CH₂), 42.2 (CH₂), 32.9 (CH₂), 26.7 (CH₃), 24.4 (CH₂), 14.0 (CH₃), 12.2 (CH₃). IR ν (Neat, cm⁻¹): 1737, 1713. HRMS (FAB⁺, M⁺+1): calcd for C₁₂H₁₇IO₃: 337.0301; found: 337.0300

1-Acetyl-3-iodo-2-phenylcyclopent-2-enecarboxylic acid ethyl ester (2e). Yellow oil. R_f = 0.38 (Hexane: AcOEt, 7:1). ¹H NMR (300 MHz, CDCl₃) δ 7.33-7.31 (m, 3H), 7.22-7.18 (m, 2H), 4.14-4.03 (m, 2H), 2.91-2.64 (m, 2H), 2.61-2.04 (m, 2H), 2.03 (s, 3H), 1.06 (t, J = 7.1, 3H). ¹³C NMR (75.5 MHz, CDCl₃) δ 203.0 (C), 170.6 (C), 145.7 (C), 136.9 (C), 129.7 (CH), 128.0 (CH), 102.3 (C), 75.0 (C), 61.9 (CH₂), 42.9 (CH₂), 33.7 (CH₂), 27.8 (CH₃), 13.9 (CH₃). IR ν (Neat, cm⁻¹): 1712. HRMS (EI): calcd for C₁₆H₁₇IO₂: 384.0217; found: 384.0219.

1-Acetyl-2-Bromo-3-iodocyclopent-2-enecarboxylic acid ethyl ester (2f). Orange oil. R_f = 0.43 (Hexane: AcOEt, 7:1). ¹H NMR (300 MHz, CDCl₃) δ 4.26 (t, J = 7.1, 2H), 2.76-2.52 (m, 4H), 2.29 (s, 3H), 1.29 (t, J = 7.1, 3H). ¹³C NMR (75.5 MHz, CDCl₃) δ 201.2 (C), 169.3 (C), 125.9 (C), 106.4 (C), 73.7 (C), 62.2 (CH₂), 42.0 (CH₂), 33.3 (CH₂), 27.5 (CH₃), 14.1 (CH₃). IR ν (Neat, cm⁻¹): 1715. HRMS (FAB⁺, M⁺+1): calcd for C₁₀H₁₃BrIO₃: 386.9093; found: 386.9090.

1-Acetyl-2,3-diiodocyclopent-2-enecarboxylic acid ethyl ester (2g). Orange oil. R_f = 0.37 (Hexane: AcOEt, 7:1). ¹H NMR (300 MHz, CDCl₃) δ 4.25 (q, J = 7.2, 2H), 2.80-2.62 (m, 3H), 2.49-2.40 (m, 1H), 2.27 (s, 3H), 1.30 (t, J = 7.1, 3H). ¹³C NMR (75.5 MHz, CDCl₃) δ 201.8 (C), 169.7 (C), 116.7 (C), 103.8 (C), 75.8 (C), 62.2 (CH₂), 44.1 (CH₂), 33.5 (CH₂), 27.7 (CH₃), 14.2 (CH₃). IR ν (Neat, cm⁻¹): 1712. HRMS (EI): calcd for C₁₀H₁₂I₂O₃: 433.8870; found: 433.8875.

1,1-Diacetyl-3-iodo-2-methylcyclopent-2-ene (2h). Brown oil. R_f = 0.28 (Hexane: AcOEt, 7:1). ¹H NMR (300 MHz, CDCl₃) δ 2.82-2.76 (m, 2H), 2.41-2.34 (m, 2H), 2.13 (s, 6H), 1.82 (t, J = 2.4, 3H). ¹³C NMR (75.5 MHz, CDCl₃) δ 205.3 (C), 140.9 (C), 100.1, 79.4 (C), 42.3 (CH₂), 31.7 (CH₂), 27.1 (CH₃), 17.7 (CH₃). IR ν (Neat, cm⁻¹): 1698. HRMS (EI): calcd for C₁₀H₁₃IO₂: 291.9955; found: 291.9953.

7-Butyl-6-iodo-5-methoxy-2-oxobicyclo[3.2.1]oct-6-ene-1-carboxylic acid ethyl ester (2i). Orange oil. R_f = 0.33 (Hexane: AcOEt, CH₂Cl₂, 14:0.75:6). ¹H NMR (300 MHz, CDCl₃) δ 4.25 (q, J = 7.2, 2H), 3.34 (s, 3H), 2.91 (dd, J = 11.4, J' = 3.3, 1H), 2.47-2.39 (m, 4H), 2.29 (d, J = 11.4, 1H), 1.94-1.84 (m, 2H), 1.37-1.34 (m, 7H), 0.91 (t, J = 7.2, 3H). ¹³C NMR (75.5 MHz, CDCl₃) δ 202.2 (C), 167.7 (C), 148.9 (C), 109.1 (C), 84.4 (C), 70.0 (C), 61.4 (CH₂), 51.6 (CH₃), 41.2 (CH₂), 34.5 (CH₂), 32.4 (CH₂), 30.5 (CH₂), 29.4 (CH₂), 23.1 (CH₂), 14.1 (CH₃), 13.8 (CH₃). IR ν (Neat, cm⁻¹): 1745, 1716. HRMS (EI): calcd for C₁₆H₂₃IO₄: 406.0635; found: 406.0642.

3a,4,5,6,7,7a-hexahydro-2-iodo-4-oxo-1H-indene-3a-carboxylic acid ethyl ester (2j). Yellow oil. R_f = 0.42 (Hexane: AcOEt, 7:1). ¹H NMR (400 MHz, CDCl₃) δ 6.25 (s, 1H), 4.23-4.06 (m, 2H), 3.21-3.11 (m, 1H), 2.83-2.77 (m, 1H), 2.57-2.54 (m, 2H), 2.41-2.27 (m, 1H), 2.04-2.01 (m, 1H), 1.95-1.86 (m, 1H), 1.85-1.79 (m, 1H), 1.65 (m, 1H), 1.22 (t, J = 7.2, 3H). ¹³C NMR (100

MHz, CDCl₃) δ 206.9 (C), 169.9 (C), 138.3 (CH), 96.5 (C), 71.7 (C), 61.8 (CH₂), 48.7 (CH₂), 45.23 (CH), 38.9 (CH₂), 26.4 (CH₂), 20.9 (CH₂), 14.1 (CH₃). IR ν (Neat, cm⁻¹): 1727, 1712. HRMS (EI): calcd for C₁₂H₁₅IO₃: 334.0060; found: 334.0061.

3a,4,5,6,7,7a-hexahydro-2-iodo-4-oxo-3-phenyl-1H-indene-3a-carboxylic acid ethyl ester (2k). Yellow oil. R_f = 0.42 (Hexane: AcOEt, 7:1). ¹H NMR (400 MHz, CDCl₃) δ 7.41-7.39 (m, 2H), 7.34-7.26 (m, 3H), 4.09-3.99 (m, 2H), 3.54-3.45 (m, 1H), 2.87-2.77 (dd, J = 16.5, J' = 7.2, 1H), 2.64 (dd, J = 16.3, J' = 8.3, 1H), 2.57-2.50 (m, 1H), 2.36-2.31 (m, 1H), 2.02-1.96 (m, 3H), 1.76-1.73 (m, 1H), 0.95 (t, J = 7.2, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 207.2 (C), 170.2 (C), 147.4

(C), 136.3 (C), 129.4 (CH), 128.0 (CH), 127.8 (CH), 98.3 (C), 73.6 (C), 61.8 (CH₂), 49.4 (CH), 47.7 (CH₂), 40.7 (CH₂), 26.4 (CH₂), 23.6 (CH₂), 13.7 (CH₃). IR ν (Neat, cm⁻¹): 1713. HRMS (EI): calcd for C₁₈H₁₉IO₃: 410.0373; found: 410.0374.

3a,4,5,6,7,7a-Hexahydro-2,3-diiodo-4-oxo-1H-indene-3a-carboxylic acid ethyl ester (2l). Yellow oil. R_f = 0.28 (Hexane: AcOEt, 7:1). ¹H NMR (400 MHz, CDCl₃) δ 4.43-4.22 (m, 2H), 3.47-3.32 (m, 1H), 2.80 (dd, J = 15.9, J' = 7.1, 1H), 2.63-2.53 (m, 1H), 2.47 (dd, J = 16.1, J' = 7.2, 1H), 2.40-2.30 (m, 1H), 1.96-1.88 (m, 2H), 1.73-1.61 (m, 2H), 1.43 (t, J = 7.2, 3H). ¹³C NMR (100 MHz, CDCl₃) δ

205.4 (C), 169.5 (C), 113.0 (C), 105.1 (C), 74.2 (C), 62.2 (CH₂), 48.8 (CH), 47.9 (CH₂), 40.0 (CH₂), 26.9 (CH₂), 22.5 (CH₂), 14.2 (CH₃). IR ν (Neat, cm⁻¹): 1712. HRMS (EI): calcd for C₁₂H₁₄I₂O₃: 459.9032; found: 459.034.

Derivatized compound **3** was prepared by Sonogashira coupling reactions of product **2a** with phenylacetylene according to method C described above.

1-acetyl-2-methyl-3-(2-phenylethynyl)cyclopent-2-enecarboxylic acid ethyl ester (3). Orange oil. R_f = 0.31 (Hexane: AcOEt, 7:1). ^1H NMR (400 MHz, CDCl_3) δ 7.46-7.43 (m, 2H), 7.32-7.29 (m, 3H), 4.22 (q, J = 7.2, 2H), 2.69-2.57 (m, 3H), 2.29-2.24 (m, 1H), 2.18 (s, 3H), 2.02 (t, J = 2.4, 3H), 1.28 (t, J = 7.1, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 203.9 (C), 170.8 (C), 143.2 (C), 131.4 (CH), 128.2 (CH), 125.0 (CH), 123.1 (C), 95.5 (C), 85.0 (C), 75.2 (C), 61.5 (CH_2), 34.2 (CH_2), 31.2 (CH_2), 26.7

(CH_3), 14.5 (CH_3), 14.0 (CH_3). IR ν (Neat, cm^{-1}): 1737, 1712. HRMS (FAB+, $\text{M}^+ + 1$): calcd for $\text{C}_{19}\text{H}_{20}\text{O}_3$: 297.1491; found: 297.1499.

Derivatized compounds **4** and **5** were prepared by Suzuki and Heck coupling reactions from product **2a** respectively (methods D and E).

Method D

Method E

Method D. Synthesis of 1-Acetyl-2-methyl-3-phenylcyclopent-2-ene carboxylic acid ethyl ester (4). To a solution of **2a** (109 mg, 0.34 mmol, 1.0 equiv), PhB(OH)_3 (45 mg, 0.37 mmol, 1.1 equiv) and CsF (141mg, 0.93 mmol, 2.7 equiv) in DME (2mL) was added $\text{Pd(PPh}_3)_4$ (15 mg, 0.013 mmol, 0.04 equiv). The resulting heterogeneous mixture was refluxed 48 h, before it was diluted with diethyl ether (15 ml). The organic layer was separated, washed with brine, dried over Na_2SO_4 , and evaporated. Chromatographic purification of the crude product (hexanes/ethyl acetate, 7/1) affords **4** as a yellow oil (70 mg, 76%). ^1H NMR (400 MHz, CDCl_3) δ 7.38-7.26 (m, 5H), 4.25 (q, J = 7.2, 2H), 2.88-2.62 (m, 3H), 2.29-2.23 (m, 1H), 2.24 (s, 3H), 1.92 (s, 3H), 1.30 (t, J = 7.2, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 205.1 (C), 171.7 (C), 142.2

(C), 137.1 (C), 131.6 (C), 129.5 (C), 128.1 (CH), 127.8 (CH), 127.1 (CH), 61.3 (CH₂), 34.4 (CH₂), 30.9 (CH₂), 26.8 (CH₃), 14.1 (CH₃), 13.9 (CH₃). IR ν (Neat, cm⁻¹): 1732, 1709. HRMS (FAB+, M⁺+1): calcd for C₁₇H₂₀O₃: 273.1491; found: 273.1497.

Method E. Synthesis of 1-Acetyl-2-methyl-3-styrylcyclopent-2-enecarboxylic acid ethyl ester (5). A mixture of **2a** (90 mg, 0.28 mmol, 1 equiv), styrene (43 mg, 0.42 mmol, 1.5 equiv), Pd(OAc)₂ (14 mg, 0.064 mmol, 0.23 equiv) and P(o-tolyl)₃ (3 mg, 0.008 mmol, 0.028 equiv) in 2 mL of Et₃N was refluxed for 48 h before it was diluted with diethyl ether (15 mL). The organic layer was separated, washed with brine, dried over Na₂SO₄, and evaporated. Chromatographic purification of the crude product (hexanes/ethyl acetate, 7/1) affords **5** as a yellow oil (64 mg, 77%). ¹H NMR (400 MHz, CDCl₃) δ 7.44 (d, *J* = 8.2, 2H), 7.33 (t, *J* = 7.47, 2H), 7.23 (t, *J* = 7.35, 1H), 7.0 (d, *J* = 16.1, 1H), 6.5 (d, *J* = 16.1, 1H), 4.23 (q, *J* = 7.1, 2H), 2.75-2.59 (m, 3H), 2.27-2.18 (m, 1H), 2.19 (s, 3H), 1.88 (s, 3H), 1.29 (t, *J* = 7.2, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 204.8 (C), 171.4 (C), 140.3 (C), 137.4 (C), 134.4 (C), 130.8 (CH), 128.6 (CH), 127.6 (CH), 126.4 (CH), 122.5 (CH), 76.6 (C), 61.3 (CH₂), 30.9 (CH₂), 30.6 (CH₂), 26.7 (CH₃), 14.1 (CH₃), 12.6 (CH₃). IR ν (Neat, cm⁻¹): 1732, 1709. HRMS (FAB+, M⁺+1): calcd for C₁₉H₂₂O₃: 299.1647; found: 299.1639.

1a

S11

1c

1b

1d

1f

dp308

S15

1g

1e

1h

1i

lj

1k

2a

2c

dpPheetociclopuro

2b

2d

2f

dp288

S27

2g

2e

2h

2j

2k

S33

¹H RMN NAV400

dp495