Supporting Information

Palladium-catalyzed [3+2] Intramolecular Cycloaddition of Alk-5-ynylidenecyclopropanes: A Rapid, Practical Approach to Bicyclo[3.3.0]octenes.

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EXPERIMENTAL SECTION

General Procedures. All dry solvents were freshly distilled under argon from an appropriate drying agent before use. Toluene and THF were distilled from sodium/benzophenone, CH_2Cl_2 and Et_3N were distilled from CaH_2 and dioxane was distilled from sodium. Pd_2dba_3 was prepared according to known literature methods.¹ Triisopropyl phosphite was purchased from Fluka and used without further purification. All reactions were conducted in dry solvents under argon atmosphere unless otherwise stated. External bath temperatures were used to record all reaction temperatures. Thin-layer chromatography (TLC) was performed on silica gel plates and components were visualised by observation under UV light, or by treating the plates with either paranylsaldehyde or cerium nitrate followed by heating. Flash chromatography was carried out in silica gel unless otherwise stated. Drying was performed with anhydrous Na_2SO_4 . Concentration refers to the removal of volatile solvents via distillation using a Buchi rotary evaporator at water aspirator pressure, followed by residual solvent removal at high vacuum (approx 0.5 mmHg).

^1H and ^{13}C NMR spectra were recorded in CDCl_3 , at 250 MHz and 62.9 MHz, respectively, and in some cases at 300 or 500 MHz (75.461 or 125.7 for ^{13}C). Carbon types were determined from DEPT- NMR experiments. The following abbreviations are used to indicate signal multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Mass spectra were acquired using a Chemical Ionization technique.

Optimization of the reaction conditions was carried out using the Agilent Technologies 6896N, Network GC System, equipped with the HP 190915-433 column and the Agilent 5976 Network Mass Selective Detector switched to the Chemical Ionization Mode.

¹ Ishii, Y.; Hasegawa, S.; Kimura, S.; Itoh, K. *J. Organomet. Chem.* **1974**, 73 (3), 411.

Preparation of diethyl 2-(2-cyclopropylideneethyl)-2-(4-hydroxybut-2-ynyl)malonate (**3b**)

To a stirred solution of the malonate **10**² (2.85 g, 12.6 mmol) in THF (40 mL) was slowly added NaH (554 mg, 15.12 mmol). The reaction mixture was allowed to stir at room temperature until no evolution of gas was observed. A solution of the tosylate **11** in 5 mL of THF was added and the resulting mixture was allowed to stir at room temperature until TLC monitoring showed complete consumption of the starting material. The reaction mixture was poured into brine and extracted with Et₂O. After drying, filtration and concentration, the crude product was purified by flash chromatography (3% EtOAc in hexanes) affording 3.4 g (80 %) of the expected coupled product as a colourless oil. This product was dissolved in 15 mL of MeOH containing *p*TsOH (358 mg, 1.8 mmol), and the mixture was warmed to 45 °C and allowed to stir overnight. The reaction mixture was poured into brine and extracted with Et₂O. After drying, filtration and concentration the crude product was purified by flash chromatography (10% EtOAc in hexanes) affording **3b** [1.90 g, 71%, colourless oil].

¹H-NMR δ (ppm): 5.59-5.52 (1H, m), 4.21-4.12 (6H, m), 2.89 (2H, d, J = 7.2 Hz), 2.78 (2H, s), 1.22 (6H, t, J = 7.1 Hz), 1.02 (br s).

¹³C-NMR δ (ppm): 170.1 (CO), 127.1 (C), 111.2 (CH), 81.3 (C), 80.6 (C), 61.5 (CH₂), 57.0 (C), 50.9 (CH₂), 34.5 (CH₂), 22.8 (CH₂), 13.9 (CH₃), 2.87 (CH₂), 1.83 (CH₂).

MS: 295 ($M+1$, 19%); 277 ($M^+-\text{H}_2\text{O}$, 100%).

HRMS: calculated for C₁₆H₂₃O₅ 295.154549, found 295.155465

² Stolle, A.; Ollivier J.; Piras, P.; Salaün, J.; de Meijere, A. *J. Am. Chem. Soc.* **1992**, *114*, 4051.

Preparation of diethyl 2-(2-cyclopropylideneethyl)-2-(4-*tert*butyldimethylsilyloxybut-2-ynyl)malonate (3a**).**

To a stirred solution of **3b** (420 mg, 1.43 mmol) in CH_2Cl_2 (5 mL) was added imidazole (117 mg, 1.72 mmol) and TBSCl (226 mg, 1.5 mmol). The reaction was allowed to stir for 10 min at rt, poured into water and extracted with CH_2Cl_2 . After drying, filtration and concentration the crude product was purified by flash chromatography (4% EtOAc in hexanes) to give **3a** [540 mg, 92%, colourless oil].

$^1\text{H-NMR}$ δ (ppm): 5.60-5.52 (1H, m), 4.24 (2H, t, $J = 2.2$ Hz), 4.16 (4H, q, $J = 6.9$ Hz), 2.89 (2H, d, $J = 7.2$ Hz), 2.79 (2H, t, $J = 2.2$ Hz), 1.22 (6H, t, $J = 7.1$ Hz), 1.05-0.98 (4H, bs), 0.87 (9H, s), 0.07 (6H, s).

$^{13}\text{C-NMR}$ δ (ppm): 170.0 (CO), 127.0 (C), 111.4 (CH), 81.4 (C), 79.7 (C), 61.4 (CH_2), 57.0 (C), 51.7 (CH_2), 34.5 (CH_2), 25.7 (C), 22.8 (CH_2), 18.2 (C), 14.0 (CH_3), 2.9 (CH_2), 1.9 (CH_2), -5.3 (CH_3).

MS: 409 (M+1, 9%); 351 (M- ^tBu , 34%), 277 (M-OTBS, 100%).

HRMS: found 409.242291 calculated 409.241028 for $\text{C}_{22}\text{H}_{37}\text{O}_5\text{Si}$

Preparation of precursors 3c-3e. General procedure exemplified for the synthesis of 3c.^{2,3}

A mixture of tosylate **5**⁴ (570 mg, 2.3 mmol), Pd₂dba₃ (24 mg, 2 mol %) and 1,2-bis(diphenylphosphino)ethane (dppe) in THF (5 mL) was stirred for 15 min at room temperature, and to the resulting mixture was added a THF solution of sodium diethyl malonate **6c**⁵ prepared by addition of NaH (250 mg, 6.25 mmol) to a stirred solution of the corresponding malonate (1.25 g, 6.3 mmol) in THF (3 mL). The reaction mixture was allowed to stir for 10 min, poured into water and extracted with ether. The combined organic layers were dried, filtered and concentrated and the crude product was purified by flash chromatography (3 to 5 % EtOAc in hexanes) to give **3c** [542 mg, 86%, colorless oil].

Diethyl 2-(2-cyclopropylideneethyl)-2-(prop-2-ynyl)malonate (3c). (colorless oil, 83% yield)

¹H-NMR δ (ppm): 5.59-5.52 (1H, m), 4.22-4.13 (4H, q, *J*= 7.01 Hz), 2.92 (2H, d, *J*= 7.2 Hz), 2.77-2.75 (2H, m), 1.98 (1H, t, *J*= 2.3 Hz), 1.26-1.19 (6H, t, *J*= 7.22 Hz), 1.03 (4H, br s).

MS: 265 (M+1, 39%); 191 (M-CO₂Et, 85%), 117 (100%).

Diethyl 2-(2-cyclopropylideneethyl)-2-(but-2-ynyl)malonate (3d). (colorless oil, 81% yield).

¹H-NMR δ (ppm): 5.50-5.43 (1H, m), 4.12-4.01 (4H, m), 2.80 (2H, d, *J*= 8.5 Hz), 2.63-2.58 (2H, m), 1.65-1.61 (3H, t, *J*= 2.5 Hz), 1.11 (6H, t, *J*= 7.2 Hz), 0.91 (4H, br s).

MS: 263 (M-15, 36%), 191 (94%), 73(100%).

³ (a) Stolle, A.; Becker, H.; Salaün, J.; de Meijere, A. *Tetrahedron Lett.* **1994**, 35, 3517.

⁴ (a) Racauchot, S.; Silvestre, I.; Olliver, J.; Kozyrkov, Y.; Pukin, A.; Kulinkovich, O.; Salaün, J. *Eur. J. Org. Chem.* **2002**, 2160. (b) Silvestre, I.; Olliver, J.; Salaün, J. *Tetrahedron. Lett.*, **2001**, 42, 4991.

⁵ Malonate precursors of **6c-6e**, were prepared according to known procedures: (a) Lawrence W. L.; Woo, H.; Smith, J.; Barrell, K. J.; Nicholls, P. J. *J. Chem. Soc. Perkin Trans I*, **1993**, 3492. (b) Brumond H. M.; Chen H.; Fisher K. D.; Kerekes A. D.; Richards B.; Still P. C.; Geib S. J. *Org. Lett.* **2002**, 4, 1931.

Diethyl 2-(2-cyclopropylideneethyl)-2-(3-trimethylsilyl-prop-2-ynyl)malonate (3e).
(colorless oil, 86% yield).

¹H-NMR δ (ppm): 5.60-5.45 (1H, m), 4.30-4.00 (4H, m), 2.93 (2H, d, *J* = 8.8 Hz), 2.79 (s, 2H), 1.23 (6H, t, *J* = 7.06 Hz), 1.05 (4H, br s), 0.12 (9H, s).

Compounds **3c**, **3d**, and **3e** have been previously described.

[2-(4-*Tert*butyldimethylsilyloxybut-2-ynyl-oxy)ethylidene]cyclopropane (7)

The coupling reaction was carried out using the same procedure than for the above malonates. Alkoxide **9** was prepared by treatment of the alcohol precursor with NaH in THF, using also the same procedure than in the case of malonates.

7 (colorless oil, 68% yield)

¹H-NMR δ (ppm): 5.94-5.88 (1H, m), 4.35 (2H, t, *J* = 1.76 Hz), 4.19 (1H, t, *J* = 1.17 Hz), 4.17-4.15 (m, 3H), 1.01 (4H, bs), 0.90 (9H, s), 0.11 (6H, s).

¹³C-NMR δ (ppm): 127.7 (C), 114.1 (CH), 89.7 (C), 80.9 (C), 69.6 (CH₂), 57.1 (CH₂), 51.7 (CH₂), 25.8 (CH₃), 18.3 (C), 2.3 (CH₂), 1.74 (CH₂), -5.2 (CH₃).

MS: 267 (M+1, 1%), 209 (M-^tBu, 2%), 183 (M-OCH₂CHC(CH₂)₂, 31%).

1-Benzyl-4,4-Diethyl- 6-cyclopropylidene-1-hexyne-1,4,4-tricarboxylate (3f)

To a cooled (-78 °C) solution of **3c** (432 mg, 1.63 mmol) in THF (5 mL) was added a 1M solution of HMDSLi in THF (2 mL, 2.0 mol). The resulting yellow solution was allowed to stir at -78 °C for 10 minutes and then a solution of benzyl chloroformate in toluene (360 μL, 2.45 mmol) was added. The resulting mixture was allowed to stir for 20 min at -78 °C, poured into saturated aqueous NH₄Cl and extracted with Et₂O. After drying, filtration and concentration the crude product was purified by flash chromatography (2 to 5% EtOAc in hexanes) to yield **3f** [465 mg, 72%, slightly yellow oil].

¹H-NMR δ (ppm): 7.33 (5H, s), 5.59-5.52 (1H, m), 5.15 (2H, s), 4.19 (4H, q, J = 7.3 Hz), 2.95-2.92 (2H, m), 1.24 (6H, t, J = 7.3 Hz), 1.05 (4H, br s).

¹³C-NMR δ (ppm): 169.1 (CO), 152.8 (CO), 134.7 (C), 128.4 (CH), 128.3 (CH), 128.2 (CH), 127.7 (C), 84.5 (C), 75.0 (C), 67.3 (CH₂), 61.8 (CH₂), 56.6 (C), 34.9 (CH₂), 22.9 (CH₂), 14.0 (CH₃), 3.05 (CH₂), 2.03 (CH₂).

MS: 399 (M+1, 9%); 307 (M-Bn, 23%); 291 (M-OBn, 100%).

HRMS: found 399.181207 calculated 399.180764 for C₂₃H₂₇O₆

Cycloaddition procedure, exemplified for the case of **3e**.

To a solution of the cyclopropene **3e** (66 mg, 0.18 mmol) in dioxane (3.6 mL) was added P(OiPr)₃ (90 μ L of a solution of 100 μ L in 1 mL of dioxane) and Pd₂dba₃ (10 mg, 6 mol %). The resulting mixture was refluxed for 30 min, using an oil bath preheated at 140°C. The crude mixture was filtrated through a short pad of celite eluting with ether. The filtrate was concentrated and purified by flash chromatography (0 to 2% AcOEt in hexanes) to afford **4e** [63 mg, 95%, slightly yellow oil].

One pot coupling-cycloaddition procedure

A solution containing the tosylate **5** (217 mg, 0.91 mmol), Pd₂dba₃ (68 mg, 8 mol %) and P(OiPr)₃ (67 μ L, 27 mol %) in dioxane (6 mL) was allowed to stir at room temperature for 30 min (until it turned green). To this mixture was added via cannula a solution of the sodium salt **6e** generated from the reaction of NaH (114 mg, 2.85 mmol) and the corresponding malonate (651 mg, 2.41 mmol) in 5 mL of dioxane. The reaction was allowed to stir at room temperature for 10 min until observing formation of the intermediate **3e** and complete consumption of the tosylate (TLC and GC monitoring). The mixture was then refluxed for 30 min until complete formation of **4e**. After standard aqueous work up the crude product was purified by flash

chromatography (0 to 1% EtOAc in hexanes) affording the cycloadduct **4e** [257 mg, 84%, slightly yellow oil].

Spectral data of the cycloadducts

Diethyl- 6-(tertbutylsilyloxymethyl)-4-methylene-1,2,3,3a,4,5-hexahydro-2,2-pentalene dicarboxylate (4a).

¹H-NMR δ (ppm): 4.89 (1H, bs), 4.82 (1H, bs), 4.23-4.0 (6H, m), 3.6-3.3 (2H, m), 3.05 (2H, m), 2.87-2.75 (1H, m), 2.61-2.53 (1H, dd, $J = 7.54$, $J = 5.02$), 1.82-1.71 (1H, m), 1.24 (6H, q, $J = 6.60$ Hz), 0.88 (9H, s), 0.04 (6H, s).

¹³C-NMR δ (ppm): 172.3 (CO), 171.6 (CO), 151.8 (C), 141.5 (C), 130.6 (C), 106.6 (CH₂), 63.1 (C), 61.5 (CH₂), 61.4 (C), 60.7 (CH₂), 54.4 (CH), 44.0 (CH₂), 37.3 (CH₂), 32.0 (CH₂), 25.9 (CH₂), 18.3 (C), 14.0 (CH₃), -5.3 (CH₃), -5.4 (CH₃).

MS: 409 (M+1, 1%), 282 (16%), 115 (65%), 75 (100%).

HRMS: found 409.241872 calculated 409.241028 for C₂₂H₃₇O₅Si

Diethyl-6-(hydroxymethyl)-4-methylene-1,2,3,3a,4,5-hexahydro-2,2-pentalene dicarboxylate (4b).

¹H-NMR δ (ppm): 4.88 (1H, bs), 4.81 (1H, bs), 4.2-4.0 (6H, m), 3.7-3.4 (2H, m), 3.17-2.97 (2H, m), 2.74 (1H, bs), 2.64 (1H, dd, $J = 8.01$ Hz, $J = 4.71$ Hz), 1.75 (1H, dd, $J = 10.84$ Hz, $J = 1.88$ Hz), 1.21 (6H, q, $J = 6.91$ Hz).

¹³C-NMR δ (ppm): 172.0 (CO), 171.8 (CO), 151.7 (C), 143.1 (C), 130.9 (C), 106.9 (CH₂), 62.7 (C), 61.6 (C), 61.5 (C), 59.8 (CH), 53.9 (CH), 43.7 (CH₂), 37.2 (CH₂), 32.0 (CH₂), 14.0 (CH₃).

MS: 295 (M+1, 26%), 279 (M-OH, 42%), 235 (50%), 61 (100%).

HRMS: found 295.154017 calculated 295.154549 for C₁₆H₂₃O₅.

Diethyl 4-methylene-1,2,3,3a,4,5-hexahydro-2,2-pentalenedicarboxylate (4c).

¹H-NMR δ (ppm): 5.37 (1H, br s), 4.89 (1H, bs), 4.83 (1H, bs), 4.24-4.13 (4H, m), 3.61-3.51 (1H, m), 3.43-3.31 (1H, m), 3.18-3.04 (1H, m), 2.99-2.78 (2H, m), 2.62 (1H, dd, $J = 8.09$ Hz, $J = 4.62$ Hz), 1.79 (1H, dd, $J = 10.87$ Hz, $J = 1.85$ Hz), 1.28-1.20 (6H, m).

¹³C-NMR δ (ppm): 172.3 (CO), 171.7 (CO), 152.9 (C), 148.3 (C), 118.7 (CH), 106.7 (CH₂), 63.0 (C), 61.5 (CH₂), 61.4 (CH₂), 53.5 (CH), 43.6 (CH₂), 37.6 (CH₂), 32.3 (CH₂), 14.0 (CH₃).

MS: 265 (M+1, 18%).

HRMS: found 265.143776 calculated 265.143984 for C₁₅H₂₁O₄

Diethyl- 6-(methyl)-4-methylene-1,2,3,3a,4,5-hexahydro-2,2-pentalene dicarboxylate (4d).

¹H-NMR δ (ppm): 4.87 (1H, bs), 4.82 (1H, bs), 4.24-4.12 (4H, m), 3.59-3.34 (2H, m), 2.97-2.83 (2H, m), 2.75-2.67 (1H, m), 2.60 (1H, dd, *J* = 7.85, 4.71 Hz), 1.76 (1H, dd, *J* = 10.84, 1.88 Hz), 1.63 (3H, s), 1.27 (6H, q, *J* = 6.59 Hz).

¹³C-NMR δ (ppm): 172.4 (CO), 171.8 (CO), 152.7 (C), 140.1 (C), 127.8 (C), 106.2 (CH₂), 63.1 (C), 61.5 (CH₂), 61.4 (CH₂), 53.9 (CH), 48.0 (CH₂), 37.9 (CH₂), 31.7 (CH₂), 14.2 (CH₃), 14.1 (CH₃), 14.0 (CH₃).

MS: 279 (M+1, 58%), 205 (M-CO₂Et, 100%)

HRMS: found 279.160214 calculated 279.159634 for C₁₆H₂₃O₄.

Diethyl- 6-(trimethylsilyl)-4-methylene-1,2,3,3a,4,5-hexahydro-2,2-pentalene dicarboxylate (4e).

¹H-NMR δ (ppm): 4.84 (1H, bs), 4.77 (1H, bs), 4.24-4.11 (4H, m), 3.65-3.56 (1H, m), 3.46-3.34 (1H, m), 3.16-3.08 (1H, m), 2.97-2.79 (2H, m), 2.64-2.55 (1H, dd, *J* = 8.01, 4.71 Hz), 1.78 (1H, dd, *J* = 11.30, 1.26 Hz), 1.23 (6H, m), 0.08 (9H, s).

¹³C-NMR δ (ppm): 172.25 (CO), 171.6 (CO), 157.8 (C), 153.7 (C), 130.8 (C), 105.4 (CH₂), 63.4 (C), 61.6 (CH₂), 61.4 (CH₂), 55.9 (CH), 47.8 (CH₂), 36.6 (CH₂), 34.1 (CH₂), 14.0 (CH₃), -1.3 (CH₃).

MS: 337 (M+1, 22%); 321 (M-CH₃, 321, 25%); 191 (100%)

HRMS: found 337.182010 calculated 337.183513 for C₁₈H₂₉O₄Si

6-Tertbutyldimethylsilyloxymethyl-4-methylene-3,3a,4,5-tetrahydro-1H-cyclopenta[c]furan (8).

¹H-NMR δ (ppm): 4.91 (1H, bs), 4.76 (1H, bs), 4.48-4.38 (1H, m), 4.30, 4.12 (3H, m), 4.08 (1H, t, *J* = 7.69 Hz), 3.92-3.78 (1H, m), 3.58-3.42 (1H, m), 3.26 (1H, dd, *J* = 7.38, 2.51 Hz), 3.16 (1H, d, *J* = 19.15 Hz), 0.90 (9H, s), 0.06 (6H, d, *J* = 1.88 Hz).

¹³C-NMR δ (ppm): 148.5 (C), 140.8 (C), 131.6 (C), 107.7 (CH), 69.2 (CH₂), 64.0 (CH₂), 61.2 (CH₂), 55.5 (CH), 25.8 (CH₃), 18.2 (C), -5.5 (CH₃).

MS: 267 (M+1, 100%), 269 (M-^tBuOH, 28%).

HRMS: found 267.178036 calculated 267.178034 for C₁₅H₂₇O₂Si.

3f

4c