Advanced Synthesis & Catalysis

Supporting Information

Supporting information

Palladium-catalyzed Intramolecular [3+2] Cycloaddition of Alkylidenecyclopropanes to allenes*

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EXPERIMENTAL PROCEDURES AND CHARACTERIZATION DATA

General procedures.

All dry solvents were freshly distilled under argon from an appropriate drying agent before use. Toluene and THF were distilled from Na/benzophenone, CH_2Cl_2 and Et_3N were distilled form CaH_2, and dioxane was distilled from Na. $Pd_2(dba)_3$ was obtained from Johnson Matthey; triisopropyl phosphite were purchased from Aldrich and tris(2,4-*t*-butylphenyl)phosphite (**L1**) and 2-(diciclohexyphosphino)biphenyl (**L3**) from Strem. Phosphoramidites **L2** and **L4** were prepared according reported procedures.[1]

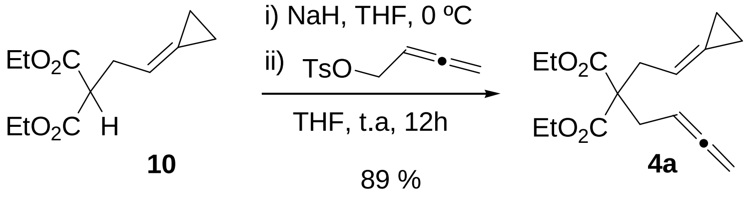
All reactions were conducted in dry solvents under argon atmosphere unless otherwise stated. External bath temperatures were used to record all reaction temperatures. Thin-layer chromatography (TLC) was performed on silica gel plates and components were visualised by observation under UV light, or by treating the plates with either *p*-anisaldehyde or cerium nitrate followed by heating. Flash chromatography was carried out on silica gel unless otherwise stated. Dryings were 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 (aprox. 0.5 mmHg).

^1H and ^{13}C NMR spectra were recorded in $CDCl_3$, at Bruker 250 MHz and Varian 300 MHz for substrates, and Varian 300 and Bruker 500 MHz for cycloadducts. Carbon types were determined from DEPT-NMR experiments. ^{31}P-NMR spectra were recorded in $CDCl_3$, at 121 MHz MHz.

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 chemical ionization (CI) or electron impact techniques (EI).

The reactions were followed by GC-MS using the Agilent Technologies 6890N, Network GC System, equipped with the Agilent 190915-433 column and the Agilent 5973 Inert Mass Selective Detector in Electron Impact or Chemical Ionization Mode (with Methane).

GENERAL PROCEDURE FOR SYNTHESIS OF SUBSTRATES 4a, 4c and 4d.



To a suspension of NaH (142 mg, 3.55 mmol) in THF (10 mL) cooled to 0ºC was added dropwise a solution of diethyl 2-(2-cyclopropylideneethyl)malonate (**10**)[2] (800 mg, 3.51 mmol) in

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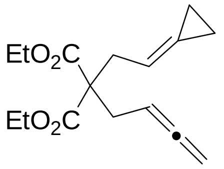
[1] J. Durán, M. Gulías, L. Castedo, J. L. Mascareñas, *Org. Lett*. **2005**, *7*, 5693- 5696.

[2] M. Gulías, R. García, A. Delgado, L. Castedo, J. L. Mascareñas *J. Am. Chem. Soc*. **2006**, *128*, 384- 385.

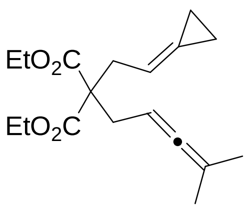
THF (10 mL). After stirring for 30 min, buta-2,3-dienyl 4-methylbenzenesulfonate[3] (1.10 mL, 4.50 mmol) was slowly added, leading to the appearance of a white precipitate. The mixture was stirred overnight at rt, poured into water and extracted with Et_2O (3x20 mL). The organic phases were dried, filtered and concentrated to give a crude oil residue that was purified by flash chromatography (5 % Et_2O/hexanes) to yield 869 mg of allene **4a** (89 %).

Diethyl 2-(buta-2,3-dienyl)-2-(2-cyclopropylideneethyl)malonate (4a)



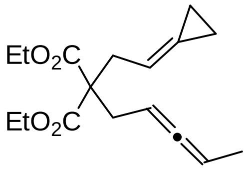
Colourless oil. **^{1}H-NMR** δ (ppm): 5.60 (1H, m), 4.97 (1H, m), 4.63 (2H, dt, *J* = 6.5 and 2.5 Hz), 4.20-4.09 (4H, m), 2.81 (2H, dd, *J* = 8.8 and 1.1 Hz), 2.60 (2H, dt, *J* = 8.0 and 2.6 Hz), 1.24 (6H, *t*, *J* = 7.1 Hz), 1.08-1.00 (4H, m); **^{13}C-NMR** δ (ppm): 209.7 (C), 170.7 (CO), 126.3 (C), 111.8 (CH), 84.4 (CH), 74.4 (CH_2), 61.2 (CH_2), 57.8 (C), 34.8 (CH_2), 31.9 (CH_2), 14.2 (CH_3), 3.0 (CH_2), 2.0 (CH_2); **MS** (CI, *m/z*, *I*): 279 ([M^+ +1], 2), 175 (5), 149 (25); **HRMS** (CI) calculated for $C_{16}H_{23}O_4$ 279.1596, found 279.1600.

Diethyl 2-(2-cyclopropylideneethyl)-2-(4-methylpenta-2,3-dienyl)malonate (4c)



Colourless oil (98 %). **^{1}H-NMR** δ (ppm): 5.61 (1H, m), 4.79 (1H, m), 4.14 (4H, q, *J* = 7.1 Hz), 2.80 (2H, d, *J* = 7.4 Hz), 2.53 (2H, d, *J* = 7.6 Hz), 1.64 (3H, s), 1.63 (3H, s), 1.22 (6H, t, *J* = 7.1 Hz), 1.04-0.96 (4H, m); **^{13}C-NMR** δ (ppm): 204.1 (C), 171.4 (CO), 126.5 (C), 112.5 (CH), 95.3 (C), 83.3 (CH), 61.4(CH_2), 58.3 (C), 34.9 (CH_2), 32.9 (CH_2), 20.9 (2xCH_3) 14.5 (CH_3), 3.2 (CH_2), 2.2 (CH_2); **MS** (CI,, *m/z*, *I*): 307 ([M^+ +1], 39), 305 (25), 261 (47), 233 (100); **HRMS** (CI) calculated for $C_{18}H_{27}O_4$ 307.1909, found 307.1905.

Diethyl 2-(2-cyclopropylideneethyl)-2-(penta-2,3-dienyl)malonate (4d)



Colourless oil (95 %). **^{1}H-NMR** δ (ppm): 5.54 (1H, m), 4.95 (1H, m), 4.84 (1H, m), 4.10 (4H, q, *J* = 7.1 Hz), 2.74 (2H, d, *J* = 6.7 Hz), 2.50 (2H, dd, *J* = 7.6 and 2.5 Hz), 1.55 (3H, dt, *J* = 5.9 and 2.9 Hz), 1.17 (6H, t, *J* = 7.1 Hz), 0.95 (4H, m); **^{13}C-NMR** δ (ppm): 206.4 (C), 170.7 (CO), 126.0 (C), 111.8 (CH), 85.2 (CH), 84.3 (CH), 60.9(CH_2), 57.7 (C), 34.4 (CH_2), 32.1 (CH_2), 14.1 (CH_3), 13.9 (CH_3), 2.7 (CH_2), 1.7 (CH_2). **MS** (EI, *m/z*, *I*): 292 ([M^+], 4), 247 (6), 219 (10), 218 (24), 189 (25), 173 (62), 145 (100). **HRMS** (EI) calculated for $C_{17}H_{24}O_4$ 292.1675, found 292.1674.

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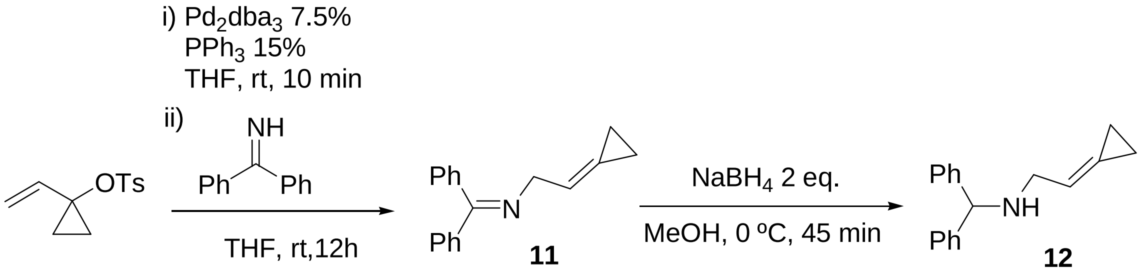
[3] This tosylate was prepared according to a reported procedure. See: Wright, M. W.; Smalley, T. L.; Welker, M. E.; Rheingold, A. L. *J. Am. Chem. Soc.* **1994**, *116*, 6777-6791. For the synthesis of substrates **4c** and **4d** the corresponding allenyl mesilates instead of the tosylates were used. For their preparation, see: Wender, P. A.; Glorius, F.; Husfeld, C. O.; Langkopf, E.; Love, J. A. *J. Am. Chem. Soc.* **1999**, *121*, 5348-5349. The allenic alcohols penta-2,3-dien-1-ol and 4-methyl-penta-2,3-dien-1-ol were prepared by standard methods: treatment of the THP ether of commercially available but-3-yn-2-ol and 2-methyl-3-butyn-2-ol with n-BuLi and p-formadehyde and subsequent exposure of the resulting product to $LiAlH_4$ in Et_2O at reflux.

PROCEDURE FOR THE PREPARATION OF AMINES 4b y 4e.

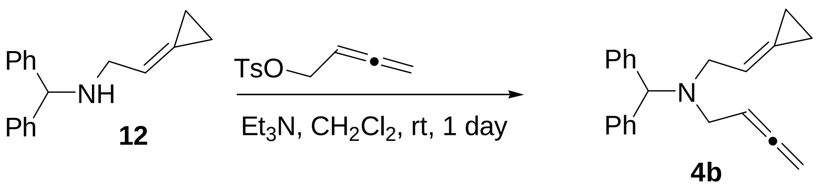
-Synthesis of N-benzhydryl-2-cyclopropylideneethanamine (**12**)



To a mixture of 1-vinylcyclopropyltosylate[1] (1.00 g, 4.19 mmol), PPh_3 (165 mg, 0.63 mmol) and Pd_2dba_3 (288 mg, 0.315 mmol) stirred for 10 minutes, was added diphenylmethanimine (1.31 g, 7.23 mmol) and the resulting solution was stirred at room temperature overnight. The mixture was poured into ice-water and extracted with Et_2O (3x30 mL). The combined organic phases were dried, filtered and concentrated and the crude oil was purified by flash chromatography (4 % EtOAc/hexanes) to give the compound **11** that was used without further purification in the next step.[4] To a solution of this imine **11** (500 mg, 2.02 mmol) in MeOH (15 mL) cooled to 0 ºC wad added $NaBH_4$ (153 mg, 5.05 mmol) and this mixture was stirred for 45 minutes. The reaction was quenched with water and extracted with Et_2O (3x30 mL). The combined organic phases were dried with Na_2SO_4, filtered and concentrated to give a crude oil which was purified by flash chromatography (5% EtOAc/hexanes) to give 405 mg of amine **12** (67 % global yield for the two steps).

^{1}H-NMR δ (ppm): 7.49-7.21 (10H, m), 5.97 (1H, m), 4.96 (1H, s), 3.42 (2H, d, J = 6.3 Hz), 1.83 (1H, s), 1.16-1.00 (4H, m); **^{13}C-NMR** δ (ppm): 144.1 (C), 128.3 (CH), 127.3 (CH), 126.8 (CH), 123.6 (C), 116.6 (CH), 66.5 (CH), 49.1 (CH_2), 1.9 (CH_2), 1.8 (CH_2). **MS** (*m/z*, *I*): 248 ([M^+], 10), 194 (1), 172 (29), 167 (100), 165 (42). **MS** (EI, *m/z*, *I*): 248 ([M^+], 14), 172 (85), 167 (100). **HRMS** (EI) calculated for $C_{18}H_{18}N$ 248.1439, found 292.1443.

-Alkylation of N-benzhydryl-2-cyclopropylideneethanamine (**12**).



To a solution of amine **12** (300 mg, 1.20 mmol) in CH_2Cl_2 (3 mL) were added Et_3N (250 μL, 1.81 mmol) and the allenyltosylate (1.08 g, 4.82 mmol). The reaction mixture was stirred at room

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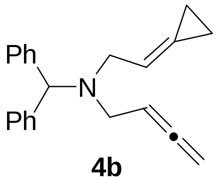
[4] Aufranc, P.; Ollivier, J.; Stolle, A.; Bremer, C.; Es-Sayed. M.; de Meijere, A.; Saläun, J. *Tetrahedron Lett.* **1993**, *34*, 4193.

temperature for 1 day, poured into water and extracted with Et_2O (3x25 mL). The organic phases were dried, filtered and concentrated. The crude oil was purified by flash chromatography (2% EtOAc/hexanes and 2% of Et_2N) to give 361 mg of the allene **4b** (99 %).

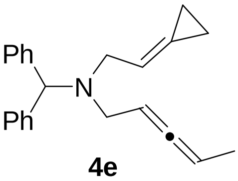
_N_-benzhydryl-_N_-(2-cyclopropylideneethyl)buta-2,3-dien-1-amine (4b)



4b

^{1}**H-NMR** δ (ppm): 7.47-7.17 (10H, m), 5.90 (1H, m), 5.18 (1H, m), 4.86 (1H, s), 4.63 (1H, m), 3.30 (2H, d, *J* = 6.6 Hz), 3.21 (2H, m), 1.11-0.88 (4H, m); ^{13}**C-NMR** δ (ppm): 209.4 (C), 142.7 (C), 128.3 (CH), 128.2 (CH), 126.8 (CH), 124.8 (C), 115.3 (CH), 86.1 (CH), 74.3 (CH_2), 70.4 (CH), 51.1 (CH_2), 48.6 (CH_2), 2.3 (CH_2), 1.9 (CH_2). **MS** (EI, *m/z*, *I*): 301 ([M^+], 43), 224 (100), 167 (52).

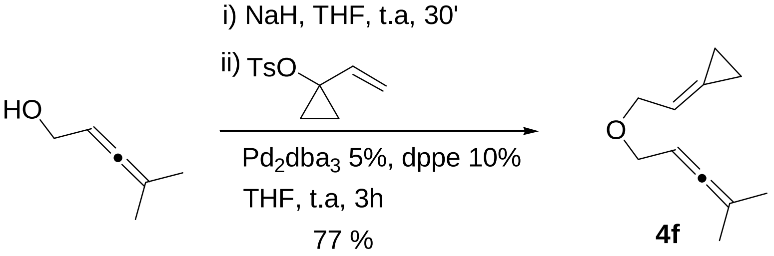
_N_-benzhydryl-_N_-(2-cyclopropylideneethyl)penta-2,3-dien-1-amine (4e)



4e

^{1}**H-NMR** δ (ppm): 7.39-7.02 (10H, m), 5.78 (1H, m), 5.08-4.86 (2H, m), 4.78 (1H, s), 3.20 (2H, s, *J* = 6.7 Hz), 3.07 (2H, dd, *J* = 6.9 and 2.2 Hz), 1.55 (3H, dd, *J* = 6.9 and 3.3 Hz), 1.02-0.77 (4H, m); ^{13}**C-NMR** δ (ppm): 205.9 (C), 142.7 (C), 128.2 (CH), 126.7 (CH), 124.7 (C), 115.4 (CH), 86.4 (CH), 85.1 (CH), 70.1 (CH), 50.9 (CH_2), 48.9 (CH_2), 14.4 (CH_3), 2.3 (CH_2), 1.9 (CH_2). **MS** (EI, *m/z*, *I*): 315 ([M^+], 9), 238 (28), 167 (100).

PREPARATION OF (2-(4-Methylpenta-2,3-dienyloxy)ethylidene)cyclopropane (4f)



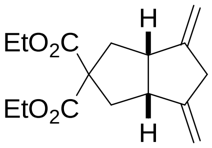
To a suspension of NaH (190 mg, 4.75 mmol) in dry THF (10 mL) at room temperature was added dropwise, 4-methylpenta-2,3-dien-1-ol (465 mg, 4.75 mmol). After stirring for 20 min at this temperature, the white suspension was sonicated for 10 minutes and stirred for another 20 minutes. Then, this mixture was added to a green solution containing Pd_2dba_3 (145 mg, 0.158 mmol), dppe (126 mg, 0.317 mmol) and the 1-vinylcyclopropyltosylate (741 mg, 3.17 mmol) in THF (10 mL), previously stirred for 20 minutes. The resulting mixture was stirred for 3h at rt, filtered through a short pad of silica gel eluting with 10% EtOAc/hexanes, concentrated and purified by flash chromatography (EtOAc/hexanes 0.5 %) to give 401 mg of the corresponding product (77 %, colourless oil).

^{1}**H-NMR** δ (ppm): 5.91 (1H, m), 5.04 (1H, m), 4.05 (2H, m), 3.92 (2H, d, *J* = 6.9 Hz), 1.68 (3H, s), 1.67 (3H, s), 1.06 (4H, m); ^{13}**C-NMR** δ (ppm): 202.8 (C), 126.6 (C), 114.8 (CH), 95.7 (C), 86.3 (CH), 69.5(CH_2), 68.6 (CH_2), 20.3 (CH_3), 2.2 (CH_2), 1.6 (CH_2). **MS** (EI, *m/z*, *I*): 164 ([M^+ -1], 1), 119 (16), 91(20), 82 (100).

GENERAL PROCEDURE FOR CYCLOADDITIONS (exemplified for substrate 4a).

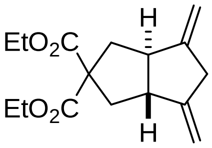
To a Schlenk tube containing deoxygenated dioxane (3.6 mL) - by three short vacuum-argon cycles - Pd_2dba_3 (3.3 mg, 3.6 μmol), **L1** (6.0 mg, 9.4 μmol) and the substrate **4a** (100 mg, 0.36 mmol) were added, ensuring that the mixture is deoxygenated after the addition of each component. The mixture was refluxed for the time indicated in the table 1 of the main manuscript. The mixture was cooled to room temperature and filtered through a short pad of silica gel eluting with EtOAc/ hexanes (10%). The filtrate was concentrated and purified by flash chromatography (1% EtOAc/hexanes) to afford **5a** (65 mg, 65 %) and **6a** (22 mg, 22%)

(3a*S**,6a*R**)-diethyl hexahydro-4,6-dimethylenepentalene-2,2(1*H*)-dicarboxylate (5a)



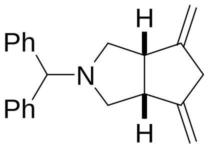
Colourless oil. **^{1}H-NMR** δ (ppm): 4.87 (2H, s), 4.84 (2H, s), 4.19 (2H, q, *J* = 7.1 Hz), 4.13 (2H, q, *J* = 7.1 Hz), 3.26-3.03 (4H, m), 2.57 (2H, m), 2.09 (2H, dd, *J* = 13.8 and 7.1 Hz), 1.25 (3H, t, *J* = 7.1 Hz), 1.22 (3H, t, *J* = 7.1 Hz); **^{13}C-NMR** δ (ppm): 172.0 (CO), 171.4 (CO), 152.8 (C), 106.6 (CH_2), 62.6 (C), 61.4 (CH_2), 61.3 (CH_2), 48.9 (CH), 40.2 (CH_2), 39.9 (CH_2), 14.0 (CH_3). **MS** (EI, *m/z*, *I*): 278 ([M^+], 12), 233 (20), 206 (27), 173 (100), 131 (96); **HRMS** (CI) calculated for $C_{16}H_{23}O_4$ 279.1596, found 279.1588.

(3a*R**,6a*R**)-diethyl hexahydro-4,6-dimethylenepentalene-2,2(1*H*)-dicarboxylate (6a)



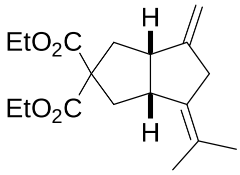
Colourless oil. **^{1}H-NMR** δ (ppm): 4.74 (4H, s), 4.24-4.12 (4H, m), 3.27 (2H, s), 2.59 (2H, m), 2.43 (2H, m), 1.82 (2H, t, *J* = 11.7 Hz), 1.26 (6H, m); **^{13}C-NMR** δ (ppm): 172.3 (CO), 147.6 (C), 103.6 (CH_2), 64.9 (C), 61.4(CH_2), 56.7 (CH), 42.9 (CH_2), 33.4 (CH_2), 14.0 (CH_3). **MS** (EI*m/z*, *I*): 278 ([M^+], 11), 233 (21), 204 (35), 173 (100), 131 (96); **HRMS** (CI) calculated for $C_{16}H_{23}O_4$ 279.1596, found 279.1595.

(3a*R**,6a*S**)-2-benzhydryl-octahydro-4,6-dimethylenecyclopenta[*c*]pyrrole (5b)



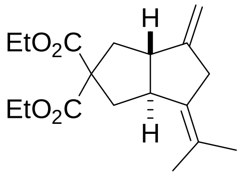
Colourless oil. **^{1}H-NMR** δ (ppm): 7.44-7.16 (10H, m), 4.88 (2H, s), 4.74 (2H, s), 4.11 (1H, s), 3.41 (1H, dd, *J* = 4.1 and 2.0 Hz), 3.16 (2H, s), 3.03 (1H, ddd, *J* = 13.8, 3.5 and 1.8 Hz), 2.66-2.63 (2H, m), 2.50 (2H, dd, *J* = 8.2 and 3.2 Hz); **^{13}C-NMR** δ (ppm): 154.2 (C), 144.0 (C), 128.4 (CH), 127.3 (CH), 126.8 (CH), 105.8 (CH_2), 75.8 (CH), 61.2 (CH), 48.4 (CH_2), 41.4 (CH_2). **MS** (*m/z*, *I*): 301 ([M^+], 14), 224 (12), 167 (100), 152 (22), 134 (32). **MS** (EI, *m/z*, *I*): 301 ([M^+], 12), 224 (14), 167 (100), 165 (58). **HRMS** calculated for $C_{22}H_{23}N$ 301.1830, found 301.1831.

(3a*S**,6a*R**)-diethyl hexahydro-4-methylene-6-(propan-2-ylidene)pentalene-2,2(1*H*)-dicarboxylate (5c)



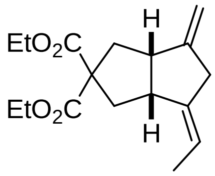
Colourless oil. **^{1}H-NMR** δ (ppm): 4.87 (1H, s), 4.82 (1H, s), 4.24-4.07 (4H, m), 3.22 (1H, m), 3.16-3.02 (3H, m), 2.59 (2H, m), 2.16 (1H, dd, *J* = 13.6 and 6.7 Hz), 1.81 (1H, m), 1.71 (3H, s), 1.59 (3H, s), 1.29-1.17 (6H, m); **^{13}C-NMR** δ (ppm): 172.1 (CO), 171.5 (CO), 154.0 (C), 135.5 (C), 123.2 (C), 106.4 (CH_2), 62.4 (C), 61.3 (CH_2), 61.2 (CH_2) 48.7 (CH), 47.0 (CH), 40.4 (CH_2), 39.6 (CH_2), 37.0 (CH_2), 21.1 (CH_3), 20.8 (CH_3), 14.0 (CH_3). **MS** (EI, *m/z*, *I*): 306 ([M^+], 57), 261 (12), 232 (41), 217 (14), 173 (100).

(3a*S,6a*S**)-diethyl hexahydro-4-methylene-6-(propan-2-ylidene)pentalene-2,2(1*H*)-dicarboxylate (6c)**



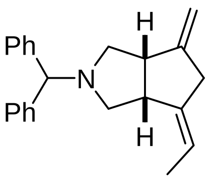
Colourless oil. **^{1}H-NMR** δ (ppm): 4.70 (1H, s), 4.67 (1H, s), 4.25-4.09 (4H, m), 3.35 (1H, m), 3.04 (1H, m), 2.82 (1H, m), 2.61-2.35 (3H, m), 1.95-1.30 (8H, m), 1.29-1.17 (6H, m). **MS** (EI, *m/z*, *I*): 306 ([M^+], 57), 261 (12), 232 (41), 217 (14), 173 (100).

(*Z*,3a*S,6a*R**)-diethyl 6-ethylidene-hexahydro-4-methylenepentalene-2,2(1*H*)-dicarboxylate (5d)[5]**



Colourless oil. **^{1}H-NMR** δ (ppm): 5.27 (1H, m); 4.88 (1H, s), 4.84 (1H, s), 4.21 (2H, q, *J* = 7.1 Hz), 4.14 (2H, q, *J* = 7.1 Hz), 3.28-3.21 (2H, m), 3.11 (1H, q, *J* = 7.8 Hz), 2.93 (1H, d, *J* = 19.5 Hz), 2.67-2.60 (2H, m), 2.09 (1H, dd, *J* = 13.5 and 7.7 Hz), 1.87 (1H, dd, *J* = 13.3 and 9.5 Hz), 1.60 (3H, d, *J* = 6.9 Hz), 1.27 (3H, t, *J* = 7.1 Hz), 1.22 (3H, t, *J* = 7.1 Hz); **^{13}C-NMR** δ (ppm): 172.0 (CO), 171.4 (CO), 153.2 (C), 143.3 (C), 116.1 (CH), 106.2 (CH_2), 62.7 (C), 61.4 (CH_2), 61.3 (CH_2), 48.6 (CH), 45.1 (CH), 40.1 (CH_2), 40.0 (CH_2), 39.4 (CH_2), 14.4 (CH_3), 14.0 (CH_3). **MS** (*m/z*, *I*): 292 ([M^+], 18), 247 (9), 218 (44), 173 (100), 145 (99). **MS** (EI, *m/z*, *I*): 292 ([M^+], 5), 263 (18), 246 (35), 218 (21), 200 (18), 189 (68), 173 (74), 172 (35), 145 (100). **HRMS** (EI) calculated for $C_{17}H_{24}O_4$ 292.1675, found 292.1689.

(*Z*,3a*R,6a*S**)-2-benzhydryl-4-ethylidene-octahydro-6-methylenecyclopenta[*c*]pyrrole (5e)**



Colourless oil. **^{1}H-NMR** δ (ppm): 7.40-7.04 (10H, m), 5.19 (1H, m), 4.73 (1H, s), 4.63 (1H, s), 4.02 (1H, s), 3.38-3.16 (2H, m), 3.06 (1H, m), 2.88-2.63 (3H, m), 2.26 (1H, dd, *J* = 9.3 and 5.1 Hz), 2.20 (1H, dd, *J* = 9.2 and 5.2 Hz), 1.41 (3H, d, *J* = 6.7 Hz); **^{13}C-NMR** δ (ppm): 154.0 (C), 144.4 (C), 144.0 (C), 128.4 (CH), 127.5 (CH), 127.3 (CH), 126.9 (CH), 126.8 (CH), 115.4 (CH), 105.6 (CH_2), 75.6 (CH), 61.2 (CH_2), 60.2 (CH_2), 48.6 (CH), 44.5 (CH), 40.8 (CH_2), 14.2 (CH_3). **MS** (EI, *m/z*, *I*): 315 ([M^+], 17), 238 (4), 167 (100).

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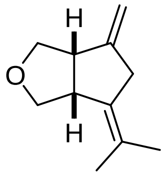
[5] The reaction was carried out with 50 mM concentration for this compound.

(3a*S**,6a*R**)-hexahydro-4-methylene-6-(propan-2-ylidene)-1*H*-cyclopenta[*c*]furan (5f)

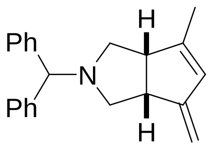


Colourless oil. **^{1}H-NMR** δ (ppm): 4.91 (1H, s), 4.84 (1H, s), 3.97 (2H, m), 3.69 (1H, dd, *J* = 8.7 and 4.5 Hz), 3.51 (1H, dd, 8.4 and 5.3 Hz), 3.37 (1H, m), 3.22 (1H, m), 1.62 (6H, s); **^{13}C-NMR** δ (ppm): 153.0 (C), 135.1 (C), 123.7 (C), 106.7 (CH_2), 74.9 (CH_2), 74.7 (CH_2), 50.5 (CH), 48.3 (CH), 37.6 (CH_2), 21.2 (CH_3), 20.8 (CH_3). **MS** (EI, *m/z*, *I*): 164 ([M^+], 43), 149 (16), 133 (27), 119 (69), 91 (100).

GENERAL PROCEDURE FOR THE Pd-CATALYZED ISOMERIZATION OF CYCLOADDUCTS (exemplified for compound 5b)

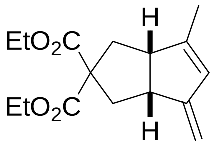
Pd_2dba_3 (2.1 mg, 2.3 μmol), ligand **L1** (3.9 mg, 6.1 μmol) and cycloadduct **5b** (14 mg, 0.047 mmol) were successively added to a Schlenk tube containing dry dioxane. This mixture was refluxed for 2h, cooled to room temperature and filtered through silica gel eluting with 10% EtOAc/hexanes. After removal the solvent the crude oil was purified by flash chromatography (0.5% EtOAc/hexanes) to give 11 mg the isomerizated product **7b** (78 %).

(3a*R**,6a*S**)-2-benzhydryl-1,2,3,3a,4,6a-hexahydro-6-methyl-4-methylenecyclopenta[*c*]pyrrole (7b)



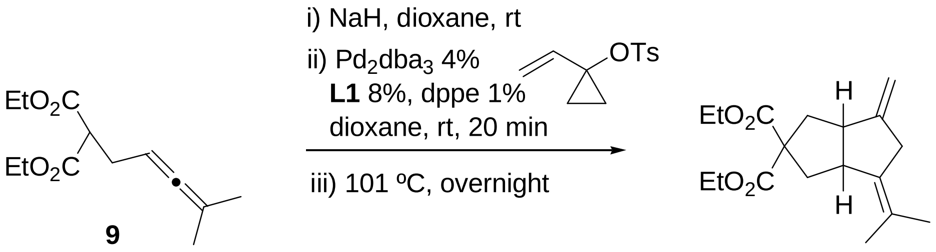
Colourless oil. **^{1}H-NMR** δ (ppm): 7.46-7.11 (10H, m), 5.87 (1H, s), 4.76 (1H, s), 4.54 (1H, s), 4.14 (1H, s), 3.31-3.18 (2H, m), 2.69 (1H, t, *J* = 8.4 Hz), 2.39 (1H, dd, *J* = 9.1 and 7.9 Hz), 2.45-2.32 (2H, m), 1.77 (3H, s); **^{13}C-NMR** δ (ppm): 158.1 (C), 150.7 (C), 143.8 (C), 129.9 (CH), 128.3 (CH), 127.2 (CH), 126.7 (CH), 100.7 (CH_2), 75.2 (CH), 60.3 (CH_2), 56.1 (CH_2), 52.5 (CH), 46.2 (CH), 15.7 (CH_3). **MS** (EI, *m/z*, *I*): 301 ([M^+], 43), 224 (3), 167 (100), 152 (17). **HRMS** (EI) calculated for $C_{22}H_{23}N$ 301.1830, found 301.1833.

(3a*R**,6a*S**)-diethyl 1,3a,4,6a-tetrahydro-6-methyl-4-methylenepentalene-2,2(1*H*)-dicarboxylate (7a)



Colourless oil. **^{1}H-NMR** δ (ppm): 5.69 (1H, s), 4.73 (1H, s), 4.62 (1H, s), 4.18 (2H, q, *J* = 7.0 Hz), 4.10 (2H, q, *J* = 7.1 Hz), 3.27-3.12 (2H, m), 2.63-2.54 (1H, m), 2.43-2.34 (1H, m), 2.12-2.02 (2H, m), 1.79 (3H, s), 1.24 (3H, t, *J* = 7.1 Hz), 1.21 (3H, t, *J* = 7.2 Hz). **^{13}C-NMR** δ (ppm): 172.0 (CO), 171.1 (C), 158.0 (C), 151.1 (C), 128.7 (CH), 101.4 (CH_2), 61.9 (C), 61.4 (CH_2), 61.2 (CH_2), 52.7 (CH), 46.3 (CH), 40.9 (CH_2), 37.0 (CH_2), 15.5 (CH_3), 14.0 (CH_3), 13.9 (CH_3). **MS** (EI, *m/z*, *I*): 278 ([M^+], 38), 233 (12), 206 (27), 173 (100), 131 (72).

PROCEDURE FOR THE TANDEM COUPLING-CYCLOADDITION:



To a suspension of NaH (9.4 mg, 0.24 mmol) in dry dioxane (1.2 mL) at 0 ºC was added dropwise, allene **9**[6] (56.6 mg, 0.24 mmol). After stirring for 10 min at this temperature, the reaction mixture was allowed to warm up to rt and stirred for further 5 min. Then, after deoxygenating (by three short vacuum-argon cycles), this mixture was added to a deoxygenated solution containing Pd$_2$dba$_3$ (8.3 mg, 0.0089 mmol), ligand **L2** (11.6, 0.0179 mmol), dppe (0.9 mg, 0.0024 mmol) and the 1-vinylcyclopropyltosylate (53.5 mg, 0.23 mmol) in dioxane (1 mL), previously stirred for 20 minutes. The resulting mixture was stirred for 1h at rt and refluxed overnight. The solution was filtered through a short pad of silica gel eluting with 10% EtOAc/hexanes, concentrated and purified (EtOAc/hexanes 0.5 %) to give a 6:1mixture of **5d** and **6d** in 62 % of yield.

STEREOCHEMICAL ANALYSIS OF THE CYCLOADDUCTS

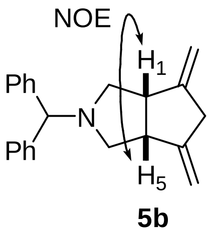
The structure of the cycloadducts was determined on the basis of two dimensional NMR experiments (COSY, NOESY, HMBC and HMQC), in addition to standard ^{1}H, ^{13}C and DEPT experiments. The stereochemistry of some of the cycloadducts and derivatives was confirmed by NOESY and NOE experiments.

Stereochemistry of 5a and 6a

The *cis*-stereochemistry of the ring-junction for compound **5a** was deduced from ^{1}H-NMR and ^{13}C-NMR data which are consistent with the existence of plane of symmetry, while for **6a** (with a *trans*-stereochemistry) NMR data are consistent with a C2- rotation axis.

Stereochemistry of 5b

For compound **5b** the *cis*-stereochemistry of the ring-junction was clearly determined from a strong NOE (NOESY) between the H1-H5 (we use this numbering to facilitate viewing)



5b

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[6] This compound was prepared for alkylation of a large excess of diethyl malonate with the corresponding mesyl allene.

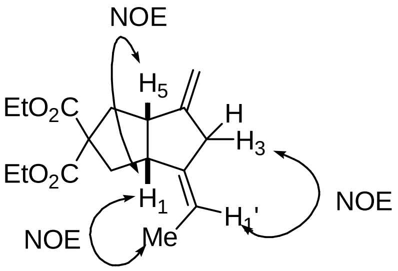
Stereochemistry of 5c and 6c

The stereochemistry of **5c** and **6c** was determined by analogy with **5a** and **6a** respectively. The *cis* fusion of cyclopentane rings of **5c** was also confirmed because it undergoes the isomerization reaction to **7c** upon further treatment under the reaction conditions, and we have observed in the case of **5a** and **6a** that only then product with *cis* fusion participates in such reaction.

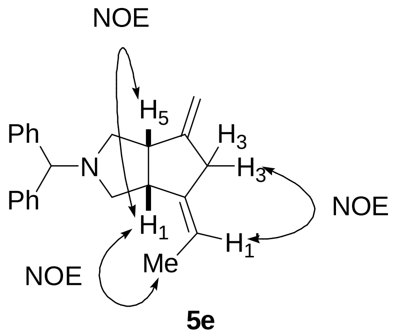
Stereochemistry of 5d and 5e

The stereochemistry of compound **5d** was determined on the basis of NOE experiments. NOE between the CH_3 group and H1 and NOE between H1' and H3 confirm the stereochemistry of the more substituted double bond while NOE between H5 and H1 confirms the *cis* fusion of ring junction.

Similarly, for compound **5e**, the *cis* fusion of cyclopentane rings was determined on basis of the presence of NOE (NOESY) between H1 and H5. And the stereochemistry of the doble bond was determined clearly because of the NOE (NOESY) of Me and H1 and H1' and one of the H3.



5d



5e

Streochemistry of 5f

The stereochemistry of this compound was determined by analogy with other NMR spectra of the cycloadducts.