**Passerini/Tsuji-Trost strategies towards lactams and cyclopentane derivatives.**

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**Experimental part:**

NMR spectra were recorded on a 400 MHz spectrometer, using deuterated solvent as reference and/or internal deuterium lock. Two-dimensional NMR spectroscopy [1H - 1H COSY spectra, 1H - 13C COSY spectra (HSQC) and long-range 1H - 13C COSY spectra (HMBC)], were carried out to determine the correlation between 1H and 13C. The chemical shifts for all NMR spectra are expressed in parts per million to high frequency of TMS reference. Coupling constants (J) are quoted in Hz and are recorded to the nearest 0.1 Hz.

The IR spectra were obtained using ATR accessories. High-resolution (HR) mass spectra were performed on a GC/MS system spectrometer. TLC was carried out using precoated plates of silica gel 60F254.

**General procedure A for Passerini reactions :**
A mixture of aldehyde (1.0 equiv), acetic acid (1.0 equiv) and isocyanide (1.0 equiv) was stirred at room temperature for 2 days. The crude was purified by flash chromatography on silica gel.

**General procedure Abis for Passerini reactions :**
A mixture of aldehyde (1.0 equiv), acetic acid (1.0 equiv) and isocyanide (1.0 equiv) was stirred at 40°C for 2 days. The crude was purified by flash chromatography on silica gel.

**General procedure B for Tsuji-Trost reactions: **
To a 0.25 M solution of Passerini adduct 1 (1.0 equiv.) in toluene were added dimethyl malonate (1.0 equiv), Cs2CO3 (1.0 equiv) and Pd(PPh3)4 (5 mol %). The resulting mixture was stirred at 50°C during 30 minutes. The solvent was removed afterwards under reduced pressure and the crude was purified by flash chromatography on silica gel.

**General procedure C for cyclisation reactions:**
To a 0.2 M solution of Tsuji-Trost adduct 2 (1.0 eq) in methanol was added Cs2CO3 (0.5eq). The resulting mixture was heated under microwave at 100°C during 30 minutes. The solvent was removed afterwards under reduced pressure. The crude was diluted with dichloromethane and the organic phase was washed with water acidified by citric acid. After drying the organic phase with MgSO4, the solvent was removed under reduced pressure. The crude was purified by flash chromatography on silica gel.

**General procedure D for Tsuji-Trost reaction followed by cyclisation for bis-nucleophiles :**
To a 0.25 M solution of Passerini adduct 1 (1.0 eq) in toluene were added the bis-nucleophile 4 (1.0 eq), Cs2CO3 (1.2 eq) and Pd(PPh3)4 (5 mol%). The resulting mixture was stirred at 50°C during 30 minutes. The solvent was removed afterwards under reduced pressure and the crude was purified by flash chromatography on silica gel.
Passerini products:

**Acetic acid 1-cyclohexylcarbamoyl-3-phenyl-allyl ester (1a)**

![Chemical structure of 1a]

Compound 1a was prepared according to general procedure A. Purification by flash chromatography with a gradient Et₂O/EP (30/70 to 100/0) gave the desired product (567 mg, 94%) as a white solid. **CCM** Rf (80/20 Et₂O/EP) = 0.36; **Mp** 129 – 130°C; **¹H-NMR (δ, ppm)** (CDCl₃, 400 MHz) 7.38 (d, J=7.6Hz, 2H), 7.31 (m, 3H), 6.72 (d, J=16.0 Hz, 1H), 6.26 (dd, J=16.0, 6.8Hz, 1H), 5.92 (d, J=7.6Hz, 1H), 5.70 (d, J=6.8Hz, 1H), 3.80 (m, 1H), 2.20 (s, 3H), 1.91 (m, 2H), 1.70 (m, 2H), 1.61 (m, 2H), 1.35 (m, 2H), 1.18 (m, 2H); **¹³C-NMR (δ, ppm)** (CDCl₃, 100.6 MHz) 169.2 (Cq), 167.1 (Cq), 135.7 (CH), 134.7 (Cq), 128.6 (2CH), 128.4 (CH), 126.9 (2CH), 122.7 (CH), 74.5 (CH), 48.3 (CH), 33.0 (2CH₂), 25.5 (CH₂), 24.81(2CH₂), 21.12 (Me); **IR (υ, cm⁻¹)** 3285, 2930, 2854, 1742, 1658, 1541, 1449, 1370, 1230, 1031; **HRMS (EI)** Calcd. for C₁₈H₂₃NO₃: 301.1678; Found: 301.1681

**Benzoic acid 1-cyclohexylcarbamoyl-3-phenyl-allyl ester (1b)**

![Chemical structure of 1b]

Compound 1b was prepared according to general procedure Abis. Purification by flash chromatography with a gradient Et₂O/EP (30/70 to 100/0) gave the desired product (880 mg, 81%) as a white solid. **CCM** Rf (80/20 Et₂O/EP) = 0.75; **Mp** 180°C; **¹H-NMR (δ, ppm)** (CDCl₃, 400 MHz) 8.12 (d, J= 7.6 Hz, 2H), 7.63 (t, J=7.2Hz, 1H), 7.50 (t, J=6.4Hz, 2H), 7.41 (d, J=8.0Hz, 2H), 7.32 (t, J=7.2Hz, 2H), 7.27 (d, J=7.6Hz, 1H), 6.81 (d, J=15.6Hz, 1H), 6.42 (dd, J=15.6, 6.8Hz, 1H), 6.02 (m, 1H), 5.99 (d, J=6.8Hz, 1H), 3.83 (m, 1H), 1.94 (m, 2H), 1.69 (m, 2H), 1.59 (m, 2H), 1.36 (m, 2H), 1.18 (m, 2H); **¹³C-NMR (δ, ppm)** (CDCl₃, 100.6 MHz) 167.2 (Cq), 165.0 (Cq), 135.7 (Ch), 133.7 (Ch), 129.8 (2Ch), 129.3 (Cq), 128.7 (2Ch), 128.5 (2Ch), 128.4 (Ch), 126.9 (2Ch), 122.7 (Ch), 74.9 (Ch), 48.3 (Ch), 33.0 (2Ch₂), 25.5 (Ch₂), 24.8 (Ch₂), 24.7 (Ch₂); **IR (υ, cm⁻¹)** 3299, 2930, 2854, 1722, 1660, 1541, 1449, 1370, 1230, 1031; **HRMS (EI)** Calcd. for C₂₃H₂₅NO₃: 363.1834; Found: 363.1834

**Acetic acid 1-tert-butylcarbamoyl-3-phenyl-allyl ester (1c)**

![Chemical structure of 1c]

Compound 1c was prepared according to general procedure A. Purification by flash chromatography with a gradient Et₂O/EP (10/90 to 30/70) gave the desired product (606 mg, 73%) as a white solid. **CCM** Rf (80/20 Et₂O/EP) = 0.55; **Mp** 116 – 118°C; **¹H-NMR (δ, ppm)** (CDCl₃, 400 MHz) 7.44 (d, J=7.6Hz, 2H), 7.37 (m, 3H), 6.76 (d, J=16.0 Hz, 1H), 6.31 (dd, J=16.0, 6.8Hz, 1H), 5.90 (br s, 1H), 5.67 (d, J=6.8Hz, 1H), 2.24 (s, 3H), 1.42 (s, 9H); **¹³C-NMR (δ, ppm)** (CDCl₃,
100.6 MHz) 169.2 (Cq), 167.1 (Cq), 135.7 (Cq), 134.7 (CH), 128.6 (2CH), 128.4 (CH), 126.8 (2CH), 122.8 (CH), 74.7 (CH), 51.5 (Cq), 28.7 (3CH3), 21.1 (CH3) ; IR (υ, cm⁻¹) 3306, 2968, 1741, 1665, 1541, 1451, 1366, 1227, 1033 ; HRMS (EI) Calcd. for C_{16}H_{21}NO_{3} : 275.1521 found : 275.1517

**Acetic acid 1-(4-chloro-benzylcarbamoyl)-3-phenyl-allyl ester (1d)**

Compound 1d was prepared according to general procedure A. Purification by flash chromatography with a gradient Et₂O/EP (30/70 to 100/0) gave the desired product (621 mg, 90%) as a cream solid. **CCM** Rf (80/20 Et₂O/EP) = 0.27 ; **Mp** 103-104°C ; **¹H-NMR** (δ, ppm) (CDCl₃, 400 MHz) 7.37 (d, J=7.6Hz, 2H), 7.30 (m, 5H), 7.21 (d, J=8.0Hz, 2H), 6.73 (d, J=15.6Hz, 1H), 6.42 (br s, 1H), 6.27 (dd, J=15.6, 6.8Hz, 1H), 5.75 (d, J=7.2Hz, 1H), 4.43 (m, 2H), 2.19 (s, 3H) ; **¹³C-NMR** (δ, ppm) (CDCl₃, 100.6 MHz) 169.3 (Cq), 168.2 (Cq), 136.2 (Cq), 135.4 (Cq), 135.1 (CH), 133.5 (Cq), 129.0 (2CH), 128.9 (2CH), 128.6 (CH), 128.5 (2CH), 126.8 (2CH), 122.1 (CH), 74.5 (CH), 42.6 (CH₂), 21.0 (CH₃) ; IR (υ, cm⁻¹) 3288, 3062, 2927, 1740, 1661, 1538, 1491, 1370, 1228, 1090, 1015 ; HRMS (EI) Calcd. for C_{19}H_{18}ClNO₃ : 343.0975 found : 343.0979

**Acetic acid 1-(4-methoxy-benzylamino)-1-oxo-4-phenylbut-3-en-2-yl acetate (1e)**

![Structure of 1e](image)

Compound 1e was prepared according to the general procedure A. Purification by flash chromatography with a gradient PE/AcOEt (from 70/30 to 50/50) as eluant gave the desired product (881 mg, 87%) as an yellow solid. **Mp** 115 – 116°C ; **¹H-NMR** (δ, ppm) (CDCl₃, 400 MHz) 7.39-7.37 (m, 2H), 7.34-7.27 (m, 3H), 7.21 (d, J= 8.6 Hz, 2H), 6.87 (d, J= 8.6 Hz, 2H), 6.73 (d, J= 15.9 Hz, 1H), 6.36 (br s, 1H), 6.29 (dd, J= 15.9, 6.8 Hz, 1H), 5.77 (dd, J= 6.8, 1.3 Hz, 1H), 4.45 (dd, J= 14.6, 5.6 Hz, 1H), 4.41 (dd, J= 14.6, 5.6 Hz, 1H), 5.77 (dd, J= 6.8, 1.3 Hz, 1H), 4.45 (dd, J= 14.6, 5.6 Hz, 1H), 4.41 (dd, J= 14.6, 5.6 Hz, 1H), 3.79 (s, 3H), 2.17 (s, 3H) ; **¹³C-NMR** (δ, ppm) (CDCl₃, 100.6 MHz) 169.2, 167.9, 159.1, 135.5, 134.9, 129.6, 129.1, 128.6, 128.4, 126.8, 122.3, 114.1, 74.5, 55.3, 42.9, 21.0 ; IR (υ, cm⁻¹) 3296, 2934, 1742, 1662, 1662, 1613, 1513, 1450, 1371, 1301, 1231, 1177, 1111, 1070, 1033 ; HRMS (EI) Calcd. for C_{19}H_{18}ClNO₃ : 339.1471 found : 339.1479

**Acetic acid 1-(3,4-dimethoxyphenethylamino)-1-oxo-4-phenylbut-3-en-2-yl acetate (1f)**

![Structure of 1f](image)

Compound 1f was prepared according to the general procedure A. Purification by flash chromatography with a gradient PE/Et₂O (from 30/70 to 0/100) as eluant gave the desired product (580 mg, 76%) as a yellow solid. **Mp** 115 – 116°C ; **¹H-NMR** (δ, ppm) (CDCl₃, 400 MHz) 7.38-7.28 (m, 5H), 6.76-6.67 (m, 4H), 6.23 (dd, J= 15.9, 6.8 Hz, 1H), 6.05 (br s, 1H), 5.70 (dd, J= 6.8, 1.0 Hz, 1H), 3.84 (s, 3H), 3.83 (s, 3H), 3.61-3.47 (m, 2H), 2.79 (dt, J= 6.6, 2.8 Hz, 2H), 2.13 (s, 3H) ; **¹³C-NMR** (δ, ppm) (CDCl₃, 100.6 MHz) 169.1, 168.0, 149.0, 147.7, 135.5, 134.7, 131.0,
128.6, 128.4, 126.8, 122.4, 120.7, 111.9, 111.2, 74.4, 55.9, 55.8, 40.5, 35.0, 20.9; **IR** (u, cm⁻¹) 3304, 2937, 1745, 1666, 1515, 1453, 1371, 1261, 1231, 1158, 1141, 1025; **HRMS** (EI) Calcd. for C₂₂H₂₅NO₅: 383.1733  found : 383.1731

**Acetic acid 1-(4-chloro-benzylcarbamoyl)-3-(4-methoxy-phenyl)-allyl ester (1g)**

Compound 1g was prepared according to general procedure A. Purification by flash chromatography with a gradient Et₂O/EP (30/70 to 100/0) gave the desired product (734 mg, 65%) as a cream solid. **CCM** Rf (80/20 Et₂O/EP) = 0.31; **Mp** 92 – 94°C; **1H-NMR** (δ, ppm) (CDCl₃, 400 MHz) 7.30 (m, 5H), 7.21 (m, 3H), 6.85 (d, J=8.8Hz, 2H), 6.69 (d, J=15.6Hz, 1H), 6.41 (br s, 1H), 6.12 (dd, J=16.0, 7.2Hz, 1H), 5.72 (d, J=7.2Hz, 1H), 4.44 (m, 2H), 3.81 (s, 3H); **13C-NMR** (δ, ppm) (CDCl₃, 100.6 MHz) 169.9 (Cq), 169.0 (Cq), 161.53 (Cq), 160.4 (Cq), 136.7 (Cq), 133.9 (Cq), 129.6 (2CH), 129.5 (2CH), 129.3 (2CH), 128.6 (2CH), 120.2 (CH), 114.5 (2CH), 75.2 (CH), 55.7 (OMe), 43.1 (CH₂), 21.4 (Me); **IR** (u, cm⁻¹) 3275, 3048, 2931, 2836, 1739, 1656, 1605, 1509, 1490, 1370, 1173, 1088, 1013; **HRMS** (EI) Calcd. for C₂₀H₂₀ClNO₄: 373.1081  found : 373.1085

**[(E)-1-((4-chlorobenzyl)amino)-4-(2-nitrophenyl)-1-oxobut-3-en-2-yl acetate (1h)]**

Compound 1h was prepared according to the general procedure A. Purification by flash chromatography with a gradient PE/AcOEt (from 70/30 to 50/50) as eluant gave the desired product (763 mg, 65%) as an yellow solid. **Mp** 106 – 107°C; **1H-NMR** (δ, ppm) (CDCl₃, 400 MHz) 7.99 (d, J= 8.1 Hz, 1H), 7.60-7.59 (m, 2H), 7.47-7.43 (m, 1H), 7.31 (d, J= 8.1 Hz, 2H), 7.23-7.17 (m, 3H), 6.50 (t, J= 5.8 Hz, 1H), 6.36 (dd, J= 15.9, 5.8 Hz, 1H), 5.85 (dd, J= 5.8, 1.3 Hz, 1H), 4.50 (dd, J= 14.9, 5.8 Hz, 1H), 4.45 (dd, J= 14.9, 5.8 Hz, 1H), 2.23 (s, 3H); **13C-NMR** (δ, ppm) (CDCl₃, 100.6 MHz) 169.1, 167.5, 147.7, 136.0, 133.5, 133.4, 131.6, 131.6, 129.0, 129.0, 128.9, 128.9, 127.9, 124.7, 73.6, 42.7, 20.9; **IR** (u, cm⁻¹) 3294, 3048, 2931, 2834, 1745, 1665, 1523, 1492, 1345, 1227, 1091, 1016; **HRMS** (EI) Calcd. for C₁₉H₁₇ClN₂O₅: 388.0826  found : 388.0824

**[(E)-1-((4-methoxybenzyl)amino)-4-(2-nitrophenyl)-1-oxobut-3-en-2-yl acetate (1i)]**

Compound 1i was prepared according to the general procedure A. Purification by flash chromatography with a gradient PE/AcOEt (from 50/50 to 40/60) as eluant gave the desired product (660 mg, 57%) as an yellow solid. **Mp** 119 – 120°C; **1H-NMR** (δ, ppm) (CDCl₃, 400 MHz) 7.97 (d, J= 8.1 Hz, 1H), 7.60-7.58 (m, 2H), 7.46-7.41 (m, 1H), 7.22 (d, J= 8.8 Hz, 2H), 7.18 (dd, J= 15.9, 1.5 Hz, 1H), 6.87 (d, J= 8.8 Hz, 2H), 6.43 (t, J= 5.5 Hz, 1H), 6.38 (dd, J= 15.9, 5.8 Hz, 1H),
5.85 (dd, J = 5.8, 1.5 Hz, 1H), 4.46 (dd, J = 14.9, 5.5 Hz, 1H), 4.41 (dd, J = 14.9, 5.5 Hz, 1H), 3.79 (s, 3H), 2.21 (s, 3H); ^13C-NMR (δ, ppm) (CDCl₃, 100.6 MHz) 169.0, 167.3, 159.1, 147.7, 133.4, 131.7, 129.5, 129.1, 128.9, 128.8, 128.6, 128.1, 124.7, 73.5, 55.3, 42.9, 20.9; IR (υ, cm⁻¹) 3299, 2936, 1744, 1667, 1517, 1346, 1234, 1175, 1036; HRMS (EI) Calcd. for C₂₀H₂₀N₂O₆: 384.1321 found: 384.1327

Acetic acid 1-(4-chloro-benzylcarbamoyl)-3-furan-2-yl-allyl ester (1j)

Compound 1j was prepared according to general procedure Abis. Purification by flash chromatography with a gradient Et₂O/EP (25/75 to 75/25) gave the desired product (451 mg, 62%) as a brown solid. CCM Rf (80/20 Et₂O/EP) = 0.44; Mp 86 – 88°C; ^1H-NMR (δ, ppm) (CDCl₃, 400 MHz) 7.36 (br s, 1H), 7.30 (d, J=8.4Hz, 2H), 7.20 (d, J=8.4Hz, 2H), 6.55 (d, J=16Hz, 2H), 6.40 (br s, 1H), 6.37 (dd, J=3.6, 2.0Hz, 1H), 6.32 (d, J=3.2Hz, 1H), 6.18 (dd, J=15.6, 6.8Hz, 1H), 5.76 (d, J=7.2Hz, 1H), 4.45 (m, 2H), 2.17 (s, 3H); ^13C-NMR (δ, ppm) (CDCl₃, 100.6 MHz) 169.3 (Cq), 168.1 (Cq), 151.2 (Cq), 142.8 (CH), 136.2 (Cq), 133.5 (Cq), 129.1 (2CH), 129.0 (2CH), 123.2 (CH), 120.4 (CH), 111.5 (CH), 110.2 (CH), 74.2 (CH), 42.7 (CH₂), 21.0 (CH₃); IR (υ, cm⁻¹) 3725, 3627, 3292, 3082, 2933, 1742, 1655, 1538, 1491, 1371, 1226, 1091, 1015; HRMS (EI) Calcd. for C₁₇H₁₆ClNO₄: 333.0768 found: 333.0771

(E)-1-(cyclohexylamino)-4-(furan-2-yl)-1-oxobut-3-en-2-yl acetate (1k)

Compound 1k was prepared according to the general procedure A. Purification by flash chromatography with a gradient PE/Et₂O (from 30/70 to 0/100) as eluant gave the desired product (267 mg, 46%) as an yellow solid. Mp 133 – 134°C; ^1H-NMR (δ, ppm) (CDCl₃, 400 MHz) 7.35 (d, J=1.8 Hz, 1H), 6.54 (d, J = 15.9 Hz, 1H), 6.37 (dd, J = 3.3, 1.8 Hz, 1H), 6.31 (d, J = 3.3 Hz, 1H), 6.16 (dd, J = 15.9, 7.1 Hz, 1H), 5.89 (d, J = 7.8 Hz, 1H), 5.67 (d, J = 7.1 Hz, 1H), 3.84-3.74 (m, 1H), 2.19 (s, 3H), 1.94-1.91 (m, 2H), 1.73-1.59 (m, 3H), 1.42-1.32 (m, 2H), 1.21-1.12 (m, 3H); ^13C-NMR (δ, ppm) (CDCl₃, 100.6 MHz) 169.1, 166.8, 151.4, 142.6, 122.8, 121.0, 111.4, 109.8, 74.2, 48.2, 33.0, 33.0, 25.4, 24.8, 21.1; IR (υ, cm⁻¹) 3287, 2930, 2858, 1744, 1655, 1546, 1453, 1371, 1230, 1155, 1107, 1021; HRMS (EI) Calcd. for C₁₆H₂₁NO₄: 291.1471 found: 291.1461

Acetic acid 1-(4-chloro-benzylcarbamoyl)-2-methyl-3-phenyl-allyl ester (1l)

Compound 1l was prepared according to the general procedure Abis. Purification by flash chromatography with a gradient Et₂O/EP (from 20/80 to 100/0) as eluant gave the desired product (804 mg, 75%) as a brown solid. CCM Rf (80/20 Et₂O/EP) = 0.25; Mp 92 – 93°C; ^1H-NMR (δ, ppm) (CDCl₃, 400 MHz) 7.36 (m, 3H), 7.31 (m, 4H), 7.25 (d, J=8.4Hz, 2H), 6.76 (s, 1H), 6.51 (br
s, 1H), 5.71 (s, 1H), 4.48 (m, 2H), 2.22 (s, 3H), 1.95 (s, 3H); $^1$H-NMR (δ, ppm) (CDCl$_3$, 100.6 MHz) 169.3 (Cq), 168.1 (Cq), 136.5 (Cq), 136.2 (Cq), 133.5 (Cq), 132.0 (Cq), 131.7 (CH), 129.2 (CH), 129.1 (4CH), 129.0 (2CH), 128.3 (2CH), 127.3 (CH), 79.2 (CH), 42.7 (CH$_2$), 21.1 (CH$_3$), 14.2 (CH$_3$); $^1$H-NMR (δ, ppm) (CDCl$_3$, 400 MHz) 7.30 (d, J = 8.3 Hz, 2H), 7.19 (d, J = 8.3 Hz, 2H), 6.29 (br s, 1H), 5.93-5.84 (m, 1H), 5.59-5.53 (m, 2H), 4.46 (dd, J = 14.9, 5.8 Hz, 1H), 4.41 (dd, J = 14.9, 5.8 Hz, 1H), 2.14 (s, 3H), 2.06 (q, J = 7.3 Hz, 2H), 1.41 (sext, J = 7.3 Hz, 2H), 0.89 (t, J = 7.3 Hz, 3H); $^1$C-NMR (δ, ppm) (CDCl$_3$, 100.6 MHz) 169.3, 168.6, 137.7, 136.3, 133.4, 129.0, 128.9, 123.3, 74.7, 42.5, 34.2, 21.8, 21.0, 13.6; IR (υ, cm$^{-1}$) 3299, 2961, 2929, 1744, 1665, 1606, 1515, 1496, 1374, 1231, 1095, 1018; HRMS (EI) Calcd. for C$_{17}$H$_{23}$NO$_4$: 305.1627 found: 305.1621

(E)-1-((4-chlorobenzyl)amino)-1-oxohept-3-en-2-yl acetate (1m)

Compound 1m was prepared according to the general procedure A. Purification by flash chromatography with a gradient PE/AcOEt (from 80/20 to 70/30) as eluant gave the desired product (647 mg, 71%) as an yellow oil. $^1$H-NMR (δ, ppm) (CDCl$_3$, 400 MHz) 7.32 (d, J = 7.6 Hz, 2H), 6.84 (d, J = 8.0 Hz, 2H), 6.66 (d, J = 16.0 Hz, 1H), 6.10 (dd, J = 16.0, 7.2 Hz, 1H), 5.84 (brs, 1H), 5.58 (d, J = 7.2 Hz, 1H), 3.79 (s, 3H), 2.18 (s, 3H), 1.36 (s, 9H); $^1$C-NMR (δ, ppm) (CDCl$_3$, 100.6 MHz) 170.0 (Cq), 168.0 (Cq), 160.4 (Cq), 135.2 (CH), 128.7 (2CH), 121.0 (CH), 114.6 (2CH), 75.6 (CH), 55.9 (CH, OMe), 52.1 (Cq, tBu), 29.3 (3CH$_3$, tBu), 21.7 (Me); IR (υ, cm$^{-1}$) 3306, 2965, 1738, 1665, 1606, 1509, 1454, 1364, 1218, 1173, 1028; HRMS (EI) Calcd. for C$_{17}$H$_{23}$NO$_4$: 305.1627 found: 305.1621

Acetic acid 1-tert-butylicarbamoyl-3-(4-methoxy-phenyl)-allyl ester (1n)

Compound 1n was prepared according to general procedure Abis. Purification by flash chromatography with a gradient Et$_2$O/EP (20/80 to 60/40) gave the desired product (358 mg, 39%) as a yellow solid. $^1$H-NMR (δ, ppm) (CDCl$_3$, 400 MHz) 7.33 (m, 2H), 7.29 (d, J = 5.2 Hz, 1H), 7.25 (m, 2H), 6.93 (1H, dd, J = 11.2 Hz, 1H), 5.78 (d, J = 15.2 Hz, 1H), 5.33 (d, J = 8.0 Hz, 1H), 4.25 (t, J = 11.2 Hz, 1H), 3.92 (d, J = 11.2 Hz, 1H), 3.82 (m, 1H), 3.77 (s, 3H), 3.50 (s, 3H), 1.92 (m, 2H), 1.72 (m, 2H), 1.63 (m,


2H), 1.35 (m, 2H), 1.15 (m, 2H); \^\textsuperscript{13}C-NMR (\textit{\delta}, ppm) (CDCl\textsubscript{3}, 100.6 MHz) 168.0 (Cq), 167.5 (Cq), 164.1 (Cq), 142.1 (CH), 138.5 (Cq), 128.9 (2CH), 127.6 (CH), 125.9 (CH), 56.9 (CH), 52.8 (CH\textsubscript{2}), 52.6 (CH\textsubscript{2}), 48.3 (CH), 48.0 (CH), 33.1 (2CH\textsubscript{2}), 25.5 (CH\textsubscript{2}), 24.8 (2CH\textsubscript{2}) ; IR (\nu, cm\textsuperscript{-1}) 3274, 2930, 2853, 1737, 1667, 1626, 1541, 1452, 1255, 1152 ; HRMS (EI) Calcd. for C\textsubscript{21}H\textsubscript{27}NO\textsubscript{5} : 373.1889 found : 373.1887

\((E)\)-dimethyl 2-(1-(\textit{\text{ tert}-butylamino})-1-oxo-4-phenylbut-3-en-2-yl)malonate (2c)

Compound 2c was prepared according to the general procedure B. by flash chromatography with a gradient PE/Et\textsubscript{2}O (from 60/40 to 50/50) as eluant gave the desired product (110 mg, 87%) as an yellow oil. \^\textsuperscript{1}H-NMR (\textit{\delta}, ppm) (CDCl\textsubscript{3}, 400 MHz) 7.32-7.28 (m, 2H), 7.25-7.20 (m, 3H), 6.87 (dd, \textit{J} = 15.2, 8.3 Hz, 1H), 5.69 (d, \textit{J} = 15.2 Hz, 1H), 5.23 (br s, 1H), 4.22 (dd, \textit{J} = 10.9, 8.3 Hz, 1H), 3.88 (d, \textit{J} = 10.9 Hz, 1H), 3.75 (s, 3H), 3.46 (s, 3H), 1.34 (s, 9H) ; \^\textsuperscript{13}C-NMR (\textit{\delta}, ppm) (CDCl\textsubscript{3}, 100.6 MHz) 167.9, 167.4, 164.3, 141.7, 138.5, 128.8, 128.2, 127.5, 126.6, 56.8, 52.8, 52.5, 51.4, 47.8, 28.7 ; IR (\nu, \text{cm}\textsuperscript{-1}) 3291, 2962, 2931, 1738, 1668, 1632, 1541, 1454, 1436, 1362, 1262, 1224, 1154 ; HRMS (EI) Calcd. for C\textsubscript{19}H\textsubscript{25}NO\textsubscript{5} : 347.1733 found : 347.1733

\((E)\)-dimethyl 2-(1-(4-chlorobenzylamino)-1-oxo-4-phenylbut-3-en-2-yl)malonate (2d)

Compound 2d was prepared according to the general procedure B. Purification by flash chromatography with a gradient PE/Et\textsubscript{2}O (from 40/60 to 20/80) as eluant gave the desired product (83 mg, 69%) as an yellow solid. Mp 86 – 87°C ; \^\textsuperscript{1}H-NMR (\textit{\delta}, ppm) (CDCl\textsubscript{3}, 400 MHz) 7.31-7.25 (m, 5H), 7.23-7.16 (m, 4H), 6.98 (dd, \textit{J} = 15.2, 8.3 Hz, 1H), 5.89 (t, \textit{J} = 5.8 Hz, 1H), 5.81 (d, \textit{J} = 15.2 Hz, 1H), 4.44 (dd, \textit{J} = 14.9, 5.8 Hz, 1H), 4.38 (dd, \textit{J} = 14.9, 5.8 Hz, 1H), 4.23 (dd, \textit{J} = 10.8, 8.3 Hz, 1H), 4.10 (d, \textit{J} = 10.8 Hz, 1H), 3.75 (s, 3H), 3.46 (s, 3H) ; \^\textsuperscript{13}C-NMR (\textit{\delta}, ppm) (CDCl\textsubscript{3}, 100.6 MHz) 167.8, 167.4, 164.3, 141.7, 138.5, 128.8, 128.2, 127.5, 126.6, 56.8, 52.8, 52.5, 51.4, 28.7 ; IR (\nu, \text{cm}\textsuperscript{-1}) 2956, 1736, 1668, 1633, 1538, 1491, 1434, 1362, 1261, 1224, 1154 ; HRMS (EI) Calcd. for C\textsubscript{22}H\textsubscript{22}ClNO\textsubscript{5} : 415.1187 found : 415.1187

\((E)\)-dimethyl 2-(1-((4-methoxybenzyl)amino)-1-oxo-4-phenylbut-2-en-1-yl)malonate (2e)

Compound 2e was prepared according to the general procedure B. Purification by flash chromatography with a gradient PE/Et\textsubscript{2}O (from 20/80 to 0/100) as eluant gave the desired product (95 mg, 78%) as an yellow oil. 1H-NMR (\textit{\delta}, ppm) (CDCl\textsubscript{3}, 400 MHz) 7.31-7.27 (m, 2H), 7.24-7.19 (m, 3H), 7.17 (d, \textit{J} = 8.6 Hz, 2H), 6.96 (dd, \textit{J} = 15.2, 8.6 Hz, 1H), 6.83 (d, \textit{J} = 8.6 Hz, 2H), 5.79-5.76 (m, 2H), 4.40 (dd, \textit{J} = 14.9, 5.8 Hz, 1H), 4.35 (dd, \textit{J} = 14.9, 5.8 Hz, 1H), 4.22 (dd, \textit{J} = 10.9, 8.6 Hz, 1H), 3.89 (d, \textit{J} = 10.9 Hz, 1H), 3.77 (s, 3H), 3.73 (s, 3H), 3.45 (s, 3H) ; \^\textsuperscript{13}C-NMR (\textit{\delta}, ppm) (CDCl\textsubscript{3}, 100.6 MHz) 167.8, 167.4, 165.0, 143.2, 138.3, 136.6, 133.3, 129.2, 128.8, 128.4, 128.1, 127.6, 125.0, 56.7, 52.8, 52.5, 47.9, 42.9 ; IR (\nu, \text{cm}\textsuperscript{-1}) 2956, 1736, 1668, 1633, 1538, 1491, 1434, 1259, 1149, 1091, 1015 ; HRMS (EI) Calcd. for C\textsubscript{22}H\textsubscript{22}ClNO\textsubscript{5} : 415.1187 found : 415.1187
Compound 2f was prepared according to the general procedure B. Purification by flash chromatography with a gradient PE/AcOEt (from 50/50 to 30/70) as eluant gave the desired product (171 mg, 72%) as an yellow solid. Mp 134 – 135°C ; $^{1}$H-NMR (δ, ppm) (CDCl$_3$, 400 MHz) 7.31-7.28 (m, 2H), 7.25-7.19 (m, 3H), 6.92 (dd, $J$ = 15.2, 8.6 Hz, 1H), 6.79 (d, $J$ = 8.1 Hz, 1H), 6.71-6.67 (m, 2H), 5.72 (d, $J$ = 15.2 Hz, 1H), 5.46 (t, $J$ = 5.6 Hz, 1H), 4.21 (dd, $J$ = 10.9, 8.6 Hz, 1H), 3.88 (d, $J$ = 10.9, 1H), 3.85 (s, 3H), 3.82 (s, 3H), 3.72 (s, 3H), 3.57-3.48 (m, 2H), 3.47 (s, 3H), 2.75 (t, $J$ = 7.1 Hz, 2H) ; $^{13}$C-NMR (δ, ppm) (CDCl$_3$, 100.6 MHz) 167.8, 167.4, 165.0, 149.0, 147.7, 142.6, 138.4, 131.2, 128.8, 128.1, 127.6, 125.4, 111.8, 111.3, 56.8, 55.9, 55.8, 52.8, 52.5, 47.9, 40.8, 35.1 ; IR (υ, cm$^{-1}$) 3285, 2957, 1737, 1670, 1628, 1544, 1517, 1454, 1433, 1321, 1291, 1234, 1196, 1147, 1029 ; HRMS (EI) Calcd. for C$_{23}$H$_{25}$NO$_6$ : 411.1682 found : 411.1691

Compound 2g was prepared according to the general procedure B. Purification by flash chromatography with a gradient Et$_2$O/PE (from 20/80 to 100/0) as eluant gave the desired product (90 mg, 75%) as an yellow solid. CCM Rf (80/20 Et$_2$O/EP) = 0.22 ; Mp 116 – 118°C ; $^{1}$H-NMR (δ, ppm) (CDCl$_3$, 400 MHz) 7.27 (d, $J$=5.6Hz, 2H), 7.18 (d, J=6.8Hz, 2H), 7.12 (d, J=7.2Hz, 2H), 6.96 (dd, J=15.2, 8.4Hz, 1H), 6.83 (d, J=7.2Hz, 2H), 5.96 (br s, 1H), 5.79 (d, J=15.2Hz, 1H), 4.44 (dd, J=11.2, 6.0 Hz, AB,1H), 4.37 (dd, J=14.2, 6.0 Hz, AB, 1H), (dd, 4.19 (t, J=9.2Hz, 1H), 3.84 (d, J=10.8Hz, 1H), 3.77 (s, 3H), 3.73 (s, 3H), 3.48 (s, 3H) ; $^{13}$C-NMR (δ, ppm) (CDCl$_3$, 100.6 MHz) 168.0 (Cq), 167.5 (Cq), 165.1 (Cq), 159.0 (Cq), 143.5 (CH), 136.6 (Cq), 133.5 (Cq), 130.22 (Cq), 129.3 (4CH), 128.8 (2CH), 124.8 (CH), 114.3 (2CH), 57.0 (CH), 55.2 (CH$_3$, OMe), 52.8 (CH$_3$, OMe), 52.6 (CH$_3$, OMe), 47.2 (CH), 43.0 (CH$_2$) ; IR (υ, cm$^{-1}$) 3275, 3066, 2957, 2838, 1735, 1666, 1631, 1511, 1434, 1248, 1178, 1091, 1031 ; HRMS (EI) Calcd. for C$_{23}$H$_{24}$ClNO$_6$ : 455.1944 found : 455.1953

(E)-dimethyl 2-4-(3,4-dimethoxyphenethylamino)-4-oxo-1-phenylbut-2-enylmalonate (2f)

Compound 2h was prepared according to the general procedure B. Purification by flash chromatography with a gradient PE/Et$_2$O (from 50/50 to 0/100) as eluant gave the desired product (80 mg, 67%) as a beige solid. Mp 57 – 58°C ; $^{1}$H-NMR (δ, ppm) (CDCl$_3$, 400 MHz) 7.78 (d, $J$=
7.6 Hz, 1H), 7.57 (t, J = 7.6 Hz, 1H), 7.41 (d, J = 7.6 Hz, 1H), 7.39 (t, J = 7.6 Hz, 1H), 7.26 (d, J = 8.1 Hz, 2H), 7.18 (d, J = 8.1 Hz, 2H), 6.94 (dd, J = 14.9, 8.6 Hz, 1H), 6.07-6.01 (m, 2H), 4.90 (dd, J = 10.9, 5.8 Hz, AB, 1H), 4.38 (dd, J = 14.9, 5.8 Hz, AB, 1H), 3.98 (d, J = 10.9 Hz, 1H), 3.72 (s, 3H), 3.49 (s, 3H) ;

\[
\text{13}^\text{C-NMR (}\delta, \text{ppm}) \quad (\text{CDCl}_3, 100.6 \text{ MHz}) \quad 167.2, 166.8, 164.7, 150.0, 140.8, 136.4, 133.3, 133.3, 133.0, 129.2, 129.2, 128.8, 128.3, 126.6, 124.7, 56.5, 53.0, 52.9, 43.0, 41.4 ;
\]

\[
\text{IR (}\nu, \text{cm}^{-1}) \quad 3282, 2953, 1740, 1670, 1636, 1524, 1493, 1437, 1356,
\]

\[
\text{HRMS (EI)} \quad \text{Calcd. for C}_{22}\text{H}_{21}\text{ClN}_2\text{O}_7 : 460.1037 \quad \text{found : 460.1035}
\]

(E)-dimethyl 2-(4-(4-chlorobenzyl)amino)-1-(2-nitrophenyl)-4-oxobut-2-en-1-yl)malonate (2i)

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\]

Compound 2i was prepared according to the general procedure B. Purification by flash chromatography with a gradient PE/AcOEt (from 50/50 to 30/70) as eluant gave the desired product (88 mg, 74%) as an yellow oil. \n
\[
\text{1}^\text{H-NMR (}\delta, \text{ppm}) \quad (\text{CDCl}_3, 400 \text{ MHz}) \quad 7.79 (d, J = 7.8 Hz, 1H), 7.57 (t, J = 7.8 Hz, 1H), 7.42 (d, J = 7.8 Hz, 1H), 7.38 (t, J = 7.8 Hz, 1H), 7.19 (d, J = 8.6 Hz, 2H), 6.93 (dd, J = 15.2, 8.6 Hz, 1H), 6.84 (d, J = 8.6 Hz, 2H), 5.98 (d, J = 15.2 Hz, 1H), 5.80 (t, J = 5.6 Hz, 1H), 4.89 (dd, J = 10.6, 8.6 Hz, 1H), 4.42 (t, J = 6.0Hz, 2H), 4.36 (t, J =9.2Hz, 1H), 3.97 (d, J = 10.6 Hz, 1H), 3.78 (s, 1H), 3.61 (s, 3H), 3.61 (s, 3H) ;
\]

\[
\text{13}^\text{C-NMR (}\delta, \text{ppm}) \quad (\text{CDCl}_3, 100.6 \text{ MHz}) \quad 167.5 (\text{C}_q), 167.4 (\text{C}_q), 164.9 (\text{C}_q), 151.2 (\text{C}_q), 142.4 (\text{CH}), 140.1 (\text{CH}), 136.6 (\text{C}_q), 133.41 (\text{C}_q), 129.3 (2\text{CH}), 128.9 (2\text{CH}), 126.2 (\text{CH}), 110.5 (\text{CH}), 107.42 (\text{CH}), 55.0 (\text{CH}), 52.9 (2\text{CH}_2), 43.0 (\text{CH}_2), 41.4 (\text{CH}) ;
\]

\[
\text{IR (}\nu, \text{cm}^{-1}) \quad 3275, 2953, 1737, 1670, 1636, 1524, 1295, 1246, 1174, 1111, 1030 ;
\]

\[
\text{HRMS (EI)} \quad \text{Calcd. for C}_{23}\text{H}_{24}\text{ClN}_2\text{O}_8 : 456.1533 \quad \text{found : 456.1545}
\]

2-[3-(4-Chloro-benzylcarbamoyl)-1-furan-2-yl-allyl]-malonic acid dimethyl ester (2j)

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Compound 2j was prepared according to the general procedure B. Purification by flash chromatography with a gradient Et\(_2\)O/Et\(_2\)O (from 20/80 to 100/0) as eluant gave the desired product (90 mg, 37%) as a yellow solid. \n
\[
\text{CCM} \quad \text{Rf (80/20 Et\(_2\)O/Et\(_2\)O) = 0.55 ; Mp 123 – 124°C ;}
\]

\[
\text{1}^\text{H-NMR (}\delta, \text{ppm}) \quad (\text{CDCl}_3, 400 \text{ MHz}) \quad 7.32 (s, 1H), 7.27 (d, J=8.4Hz, 2H), 7.18 (d, J=8.4Hz, 2H), 6.90 (dd, J=15.2, 8.4Hz, 1H), 6.27 (s, 1H), 6.13 (s, 1H), 5.92 (br s, 1H), 5.87 (d, J=14.8Hz, 1H), 4.42 (t, J=6.0Hz, 2H), 4.36 (t, J=9.2Hz, 1H), 3.89 (d, J=10.4Hz, 1H), 3.71 (s, 3H), 3.61 (s, 3H) ;
\]

\[
\text{13}^\text{C-NMR (}\delta, \text{ppm}) \quad (\text{CDCl}_3, 100.6 \text{ MHz}) \quad 167.5 (\text{C}_q), 167.4 (\text{C}_q), 164.9 (\text{C}_q), 151.2 (\text{C}_q), 142.4 (\text{CH}), 140.1 (\text{CH}), 136.6 (\text{C}_q), 133.41 (\text{C}_q), 129.3 (2\text{CH}), 128.9 (2\text{CH}), 126.2 (\text{CH}), 110.5 (\text{CH}), 107.42 (\text{CH}), 55.0 (\text{CH}), 52.9 (2\text{CH}_2), 43.0 (\text{CH}_2), 41.4 (\text{CH}) ;
\]

\[
\text{IR (}\nu, \text{cm}^{-1}) \quad 3275, 2953, 1737, 1670, 1636, 1524, 1491, 1434, 1252, 1163, 1092, 1014 ;
\]

\[
\text{HRMS (EI)} \quad \text{Calcd. for C}_{20}\text{H}_{20}\text{ClNO}_6 : 405.0979 \quad \text{found : 405.0987}
\]

(E)-dimethyl 2-(1-(cyclohexylamino)-4-(furan-3-yl)-1-oxobut-3-en-2-yl)malonate (2k)

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\]
Compound 2k was prepared according to the general procedure B. Purification by flash chromatography with a gradient PE/Et<sub>2</sub>O (from 70/30 to 20/80) as eluant gave the desired product (92 mg, 74%) as an yellow solid. Mp 141 – 142°C ; <sup>1</sup>H-NMR (δ, ppm) (CDCl<sub>3</sub>, 400 MHz) 7.33 (d, J = 1.8 Hz, 1H), 6.83 (dd, J = 15.2, 8.3 Hz, 1H), 6.28 (dd, J = 3.3, 1.8 Hz, 1H), 6.14 (d, J = 3.3 Hz, 1H), 5.81 (d, J = 15.2 Hz, 1H), 5.34 (br s, 1H), 4.36 (dd, J = 10.3 Hz, 1H), 3.90 (d, J = 10.3 Hz, 1H), 3.85-3.75 (m, 1H), 3.73 (s, 3H), 3.62 (s, 3H), 1.93-1.89 (m, 2H), 1.71-1.59 (m, 3H), 1.40-1.31 (m, 2H), 1.19-1.07 (m, 3H) ; <sup>13</sup>C-NMR (δ, ppm) (CDCl<sub>3</sub>, 100.6 MHz) 167.5, 167.4, 163.9, 151.4, 142.3, 138.9, 126.9, 110.4, 107.2, 55.0, 52.8, 48.3, 41.4, 33.1, 25.5, 24.8 ; IR (υ, cm<sup>-1</sup>) 3280, 2933, 2859, 1741, 1669, 1628, 1546, 1453, 1436, 1347, 1261, 1152, 1011 ; HRMS (EI) Calcd. for C<sub>19</sub>H<sub>25</sub>NO<sub>6</sub>: 363.1682 found : 363.1687

2-[3-(4-Chloro-benzylcarbamoyl)-2-methyl-1-phenyl-allyl]-malonic acid dimethyl ester (2l)

Compound 2l was prepared according to the general procedure B. Purification by flash chromatography with a gradient Et<sub>2</sub>O/PE (from 20/80 to 100/0) as eluant gave the desired product (103 mg, 57%) as an yellow solid. CCM Rf (50/50 Et<sub>2</sub>O/EP) = 0.11 ; Mp 68°C ; <sup>1</sup>H-NMR (δ, ppm) (CDCl<sub>3</sub>, 400 MHz) 7.29 (m, 4H), 7.20 (m, 5H), 5.79 (s, 1H), 5.75 (br s, 1H), 4.42 (d, J=5.6Hz, 2H), 4.14 (d, J=12.0Hz, AB system, 1H), 4.11 (d, J=12.0Hz, AB system, 1H), 3.73 (s, 3H), 3.48 (s, 3H), 2.06 (s, 3H) ; <sup>13</sup>C-NMR (δ, ppm) (CDCl<sub>3</sub>, 100.6 MHz) 168.1 (Cq), 167.6 (Cq), 166.1 (Cq), 153.0 (Cq), 137.8 (Cq), 136.9 (Cq), 133.3 (Cq), 129.3 (2CH), 128.9 (2CH), 128.7 (2CH), 128.1 (2CH), 127.7 (CH), 118.7 (CH), 55.1 (CH), 54.4 (CH), 53.0 (CH<sub>3</sub>), 42.8 (CH<sub>2</sub>), 17.0 (CH<sub>3</sub>) ; IR (υ, cm<sup>-1</sup>) 3293, 2951, 1736, 1635, 1524, 1433, 1091 ; HRMS (EI) Calcd. for C<sub>23</sub>H<sub>24</sub>ClNO<sub>5</sub>: 429.1343 found : 429.1339

(E)-dimethyl 2-(1-((4-chlorobenzyl)amino)-1-oxohept-2-en-4-yl)malonate (2m)

Compound 2m was prepared according to the general procedure B. Purification by flash chromatography with a gradient PE/AcOEt (from 60/40 to 50/50) as eluant gave the desired product (53 mg, 43%) as a white solid. Mp 146 – 147°C ; <sup>1</sup>H-NMR (δ, ppm) (CDCl<sub>3</sub>, 400 MHz) 7.30 (d, J = 8.3 Hz, 2H), 7.22 (d, J = 8.3 Hz, 2H), 6.64 (dd, J = 15.2, 9.9 Hz, 1H), 5.85 (d, J = 15.2 Hz, 1H), 5.79 (br s, 1H), 4.48 (dd, J = 15.2, 5.8 Hz, AB, 1H), 4.43 (dd, J = 15.2, 5.8 Hz, AB,1H), 3.74 (s, 3H), 3.67 (s, 3H), 3.44 (d, J = 9.1 Hz, 1H), 2.97-2.89 (m, 1H), 1.48-1.30 (m, 3H), 1.26-1.16 (m, 1H), 0.87 (t, J = 7.1 Hz, 3H) ; <sup>13</sup>C-NMR (δ, ppm) (CDCl<sub>3</sub>, 100.6 MHz) 168.3, 168.2, 165.0, 143.8, 136.6, 133.3, 129.2, 128.8, 125.8, 56.0, 52.6, 52.4, 42.9, 42.1, 34.1, 20.2, 13.7 ; IR (υ, cm<sup>-1</sup>) 3286, 2956, 2932, 1737, 1668, 1623, 1531, 1492, 1434, 1301, 1255, 1173, 1150, 1092, 1016 ; HRMS (EI) Calcd. for C<sub>19</sub>H<sub>25</sub>ClNO<sub>5</sub>: 381.1343 found : 381.1349

dimethyl 2-(1-(4-chlorobenzyl)-5-oxo-2-phenylpyrrolidin-2-yl)malonate (3d)
Compound 3d was prepared according to the general procedure C. Purification by flash chromatography with a gradient PE/Et$_2$O (from 20/80 to 30/70) as eluant gave the desired product (39 mg, 33%) as an yellow oil. $^1$H-NMR (δ, ppm) (CDCl$_3$, 400 MHz) 7.25-7.15 (m, 5H), 7.07 (d, J = 8.3 Hz, 2H), 4.39 (s, 1H), 4.25 (d, J = 15.2 Hz, 1H), 4.01 (d, J = 15.2 Hz, 1H), 3.66 (s, 3H), 3.57 (s, 3H), 3.36-3.28 (m, 1H), 2.70-2.66 (m, 2H), 2.60-2.52 (m, 1H); $^{13}$C-NMR (δ, ppm) (CDCl$_3$, 100.6 MHz) 175.9, 167.1, 167.0, 142.6, 136.1, 132.8, 130.1, 128.7, 128.1, 121.5, 69.1, 55.1, 52.9, 52.8, 44.0, 30.4, 29.9; IR (υ, cm$^{-1}$) 2953, 1754, 1733, 1678, 1492, 1434, 1395, 1328, 1265, 1203, 1142, 1092, 1016; HRMS (EI) Calcd. for C$_{22}$H$_{22}$ClNO$_5$: 415.1187 found: 415.1184.

2-[1-(4-Methoxy-benzyl)-5-oxo-2-phenyl-pyrrolidin-2-yl]-malonic acid dimethyl ester (3e)

Compound 3e was prepared according to the general procedure C. Purification by flash chromatography with a gradient Et$_2$O/PE (from 20/80 to 100/0) as eluant gave the desired product (63 mg, 38%) as an yellow oil. $^1$H-NMR (δ, ppm) (CDCl$_3$, 400 MHz) 7.20 (m, 3H), 6.91 (d, J=8.8Hz, 2H), 6.85 (t, J=8.8Hz, 2H), 6.65 (d, J=8.8 Hz, 2H), 4.39 (s, 1H), 4.31 (d, J=15.2Hz, 2H), 6.73 (s, 3H), 6.66 (s, 3H), 6.53 (s, 3H), 3.32 (m, AB system, 1H), 2.68 (m, 2H), 2.54 (m, AB system, 1H); $^{13}$C-NMR (δ, ppm) (CDCl$_3$, 100.6 MHz) 175.9 (Cq), 167.3 (Cq), 167.2 (Cq), 158.6 (Cq), 142.9 (Cq), 130.1 (2CH), 128.7 (2CH), 128.1 (CH), 126.1 (2CH), 113.5 (2CH), 69.2 (Cq), 55.3 (CH$_3$), 55.1 (CH), 52.9 (CH$_3$), 52.8 (CH$_3$), 44.0 (CH$_2$), 30.5 (CH$_2$), 30.1 (CH$_2$); IR (υ, cm$^{-1}$) 3293, 2951, 2836, 1731, 1662, 1509, 1398, 1240, 1113, 1028; HRMS (EI) Calcd. for C$_{23}$H$_{25}$NO$_6$: 411.1682 found: 411.1684.

2-[1-(4-Chloro-benzyl)-2-(4-methoxy-phenyl)-5-oxo-pyrrolidin-2-yl]-malonic acid dimethyl ester (3g)

Compound 3g was prepared according to the general procedure C. Purification by flash chromatography with a gradient Et$_2$O/PE (from 20/80 to 100/0) as eluant gave the desired product (64 mg, 64%) as an yellow oil. $^1$H-NMR (δ, ppm) (CDCl$_3$, 400 MHz) 7.08 (m, 4H), 6.90 (d, J=8.4Hz, 2H), 6.73 (d, J=8.4Hz, 2H), 4.35 (s, 1H), 4.17 (d, J=15.2Hz, AB system, 1H), 4.03 (d, J=15.2Hz, AB system, 1H), 3.77 (s, 3H), 3.66 (s, 3H), 3.56 (s, 3H), 3.30...
(m, AB system, 1H), 2.65 (t, J=8.8Hz, 2H), 2.52 (m, AB system, 1H); 13C-NMR (δ, ppm) (CDCl3, 100.6 MHz) 175.8 (Cq), 167.2 (Cq), 167.1 (Cq), 159.2 (Cq), 136.4 (Cq), 134.4 (Cq), 132.7 (Cq), 130.1 (2CH), 128.1 (2CH), 127.3 (2CH), 113.9 (2CH), 68.8 (Cq), 55.4 (CH3), 55.1 (CH), 52.9 (CH3), 52.8 (CH3), 30.2 (CH2), 30.0 (CH2); IR (υ, cm⁻¹) 2952, 2838, 1754, 1733, 1671, 1513, 1450, 1433, 1249, 1188, 1088, 1015; HRMS (EI) Calcd. for C23H24ClNO6: 445.1292 found: 445.1292

2-[1-(4-Chloro-benzyl)-2-furan-2-yl-5-oxo-pyrrolidin-2-yl]-malonic acid dimethyl ester (3j)

Compound 3j was prepared according to the general procedure C. Purification by flash chromatography with a gradient Et2O/PE (from 20/80 to 100/0) as eluant gave the desired product (48 mg, 53%) as an yellow oil. CCM Rf (80/20 Et2O/EP) = 0.32; 1H-NMR (δ, ppm) (CDCl3, 400 MHz) 7.22 (s, 1H), 7.12 (d, J=8.4Hz, 2H), 6.98 (d, J=8.0 Hz, 2H), 6.23 (s, 1H), 6.21 (s, 1H), 4.32 (d, J=15.6Hz, AB system, 1H), 4.30 (s, 1H), 4.24 (d, J=15.6Hz, AB system, 1H), 3.64 (s, 3H), 3.56 (s, 3H), 3.21 (m, 2H), 2.61 (m, 2H); 13C-NMR (δ, ppm) (CDCl3, 100.6 MHz) 175.6 (Cq), 166.5 (Cq), 166.4 (Cq), 153.2 (Cq), 142.5 (CH), 135.9 (Cq), 132.8 (Cq), 129.5 (2CH), 128.3 (2CH), 110.6 (CH), 108.0 (CH), 65.1 (Cq), 54.1 (CH), 53.0 (CH3), 52.9 (CH3), 43.5 (CH2), 29.5 (CH2), 26.1 (CH2); IR (υ, cm⁻¹) 3725, 3627, 3307, 2952, 1734, 1669, 1434, 1399, 1328, 1149, 1089, 1015; HRMS (EI) Calcd. for C20H20ClNO6: 405.0979 found: 405.0982

2,4-Bis-methoxycarbonyl-pentanedioic acid dimethyl ester (4)

A mixture of dimethylmalonate (5.5 mL, 2.4eq), diiodomethane (1eq) and potassium carbonate (2.4 equiv) in 50 mL of DMF was stirred at room temperature during 24h, then at 100°C during 4h. 150 mL of diethyl ether was added. The crude was filtrated, washed with diethylether. The filtrate was washed with 2*50 mL of water and 50mL of brine, and dried with MgSO4. The crude was purified by silica gel column chromatography with a gradient of AcOEt in EP (10:90 to 30:70), to afford 2.66g of uncolored oil (48% yield). CCM Rf (30/70 AcOEt/EP) = 0.39; 1H-NMR (δ, ppm) (CDCl3, 400 MHz) 3.74 (s, 12H), 3.50 (t, J=7.6 Hz, 2H), 2.48 (t, J=7.6 Hz, 2H); 13C-NMR (δ, ppm) (CDCl3, 100.6 MHz) 3.74 (4Cq), 3.50 (2CH), 2.48 (2CH); IR (υ, cm⁻¹) 3725, 3627, 3307, 2952, 274 (CH2); HRMS (EI) Calcd. for C11H16O8: 276.0845 found: 276.0847

4-(tert-Butylcarbamoyl-methyl)-5-phenyl-cyclopentane-1,1,3,3-tetracarboxylic acid tetramethyl ester (5c)
Compound 5c was prepared according to the general procedure D. Purification by flash chromatography with a gradient Et<sub>2</sub>O/PE (from 50/50 to 70/30) as eluant gave the desired product (140 mg, 78%) as a yellow oil. CCM Rf (70/2=30 Et<sub>2</sub>O/EP) = 0.36; <sup>1</sup>H-NMR (δ, ppm) (CDCl<sub>3</sub>, 400 MHz) 7.21 (m, 5H), 5.67 (br s, 1H), 3.89 (d, J=13.2 Hz, 1H), 3.78 (s, 3H), 3.70 (br s, 6H), 3.51 (m, 1H), 3.15 (d, J=16.0Hz, AB system, 1H), 3.08 (s, 3H), 2.95 (d, J=16.0Hz, AB system, 1H), 2.41 (dd, J<sub>1</sub>=14.8, 6.4 Hz, AB, 1H), 1.94 (dd, J<sub>1</sub>=16.0, 4.8 Hz, AB, 1H), 1.13 (s, 9H); <sup>13</sup>C-NMR (δ, ppm) (CDCl<sub>3</sub>, 100.6 MHz) 171.8 (Cq), 171.2 (Cq), 170.9 (Cq), 170.5 (Cq), 169.6 (Cq), 136.4 (Cq), 128.2 (4CH), 127.7 (CH), 63.4 (Cq), 61.2 (Cq), 55.1 (CH), 53.1 (CH<sub>3</sub>), 52.9 (CH<sub>3</sub>), 52.8 (CH<sub>3</sub>), 52.4 (CH<sub>3</sub>), 50.8 (Cq), 46.1 (CH), 41.6 (CH<sub>2</sub>), 38.2 (CH<sub>2</sub>), 28.5 (3CH<sub>3</sub>); IR (υ, cm<sup>-1</sup>) 3395, 2954, 1727, 1666, 1530, 1433, 1208, 1077; HRMS (EI) Calcd. for C<sub>25</sub>H<sub>33</sub>NO<sub>9</sub>: 491.2155 found: 491.2161

3-(4-Chloro-benzyl)-6-(4-methoxy-phenyl)-1,4-dioxo-tetrahydro-cyclopenta[e][1,2]oxazepine-7,7,8a-tricarboxylic acid trimethyl ester (5g)

Compound 5g was prepared according to the general procedure D. Purification by flash chromatography with a gradient AcOEt/PE (from 10/90 to 50/50) as eluant gave the desired product (159 mg, 67%) as white crystals. CCM Rf (50/50 AcOEt/EP) = 0.37; Mp 134 – 136°C; <sup>1</sup>H-NMR (δ, ppm) (CDCl<sub>3</sub>, 400 MHz) 7.27 (s, 4H), 7.10 (d, J=8.8Hz, 2H), 7.07 (d, J=8.8 Hz, 2H), 5.01 (d, J=14.4Hz, AB system, 1H), 4.92 (d, J=14.4Hz, AB system, 1H), 3.82 (d, J=12.0, 5.6 Hz, 1H), 3.77 (s, 3H), 3.73 (s, 3H), 3.70 (s, 3H), 3.51 (d, J=14.8 Hz, AB system, 1H), 3.14 (s, 3H), 3.09 (dd, J=12.0, 5.6 Hz, 1H), 2.86 (dd, J=18.4, 6.4 Hz, AB system, 1H), 2.54 (dd, J=18.4, 6.4 Hz, AB system, 1H); <sup>13</sup>C-NMR (δ, ppm) (CDCl<sub>3</sub>, 100.6 MHz) 171.6 (Cq), 170.0 (2Cq), 169.9 (Cq), 169.4 (Cq), 159.3 (Cq), 135.1 (Cq), 133.3 (Cq), 130.0 (2CH), 129.9 (2CH), 128.5 (2CH), 127.4 (Cq), 114.0 (2CH), 63.0 (Cq), 58.5 (Cq), 55.3 (CH<sub>3</sub>), 53.6 (CH<sub>3</sub>), 53.5 (CH<sub>3</sub>), 53.3 (CH), 52.6 (CH<sub>3</sub>), 43.2 (CH<sub>2</sub>), 42.3 (CH), 40.8 (CH<sub>2</sub>), 31.1 (CH<sub>2</sub>); IR (υ, cm<sup>-1</sup>) 3002, 2953, 2840, 1726, 1677, 1610, 1514, 1433, 1089; HRMS (EI) Calcd. for C<sub>29</sub>H<sub>32</sub>ClNO<sub>10</sub>: 589.1715 found: 589.1721

4-(tert-Butylcarbamoyl-methyl)-5-(4-methoxy-phenyl)-cyclopentane-1,1,3,3-tetracarboxylic acid tetramethyl ester (5n)
Compound 5n was prepared according to the general procedure D. Purification by flash chromatography with a gradient AcOEt/PE (from 10/90 to 30/70) as eluant gave the desired product (99 mg, 58%) as an uncolored oil. 

**CCM** Rf (50/50 AcOEt/EP) = 0.33; $^1$H-NMR (δ, ppm) (CDCl$_3$, 400 MHz) 7.21 (d, J=8.8 Hz, 2H), 6.78 (d, J=8.8 Hz, 2H), 5.71 (br s, 1H), 3.85 (d, J=13.2 Hz, 1H), 3.74 (s, 6H), 3.73 (s, 3H), 3.47 (m, 1H), 3.18 (s, 3H), 3.15 (d, J=14.8 Hz, 1H), 2.96 (d, J=14.8 Hz, AB system, 1H), 2.41 (dd, J=14.8, 6.8 Hz, 2H), 1.95 (dd, J=15.2, 6.8 Hz, 2H), 1.17 (s, 9H); $^{13}$C-NMR (δ, ppm) (CDCl$_3$, 100.6 MHz) 171.9 (Cq), 171.3 (Cq), 171.0 (Cq), 170.7 (Cq), 169.7 (Cq), 159.0 (Cq), 130.34 (2CH), 128.2 (Cq), 113.6 (2CH), 63.3 (Cq), 61.2 (Cq), 55.2 (CH$_3$), 54.3 (CH), 53.1 (CH$_3$), 52.9 (CH$_3$), 52.8 (CH$_3$), 52.6 (CH$_3$), 50.9 (Cq), 46.1 (CH), 41.5 (CH$_3$), 38.2 (CH$_2$), 28.6 (3CH$_3$); IR (υ, cm$^{-1}$) 3637, 3396, 2954, 2839, 1727, 1661, 1611, 1513, 1433, 1208, 1178, 1078; HRMS (EI) Calcd. for C$_{26}$H$_{35}$NO$_{10}$: 521.2265 found: 521.2265

2-(1-Phenyl-ethylidene)-malononitrile (6)

A mixture of acetophenone (5.6 mL, 1 eq), malononitrile (1 eq) and ammonium acetate (1.88 eq) in toluene (1 M) was stirred during 6h at reflux. The crude was diluted in Et$_2$O and extracted with water and dried with MgSO$_4$. The crude was purified by silica gel column chromatography with a gradient of Et$_2$O in EP (20:80 to 30:70), to afford 2.19 g of pale yellow solid (27% yield). 

**CCM** Rf (50/50 Et$_2$O/EP) = 0.26; Mp 98 – 99°C; $^1$H-NMR (δ, ppm) (CDCl$_3$, 400 MHz) 7.54 (m, 5H), 2.64 (s, 3H); $^{13}$C-NMR (δ, ppm) (CDCl$_3$, 100.6 MHz) 175.6 (Cq), 135.9 (Cq), 132.3 (CH), 129.2 (2CH), 127.4 (2CH), 112.9 (Cq), 112.8 (Cq), 84.7 (Cq), 24.3 (CH$_3$); IR (υ, cm$^{-1}$) 3067, 2226, 1583, 1564, 1491, 1440, 1376, 1306, 1190, 1051; HRMS (EI) Calcd. for C$_{11}$H$_8$N$_2$: 168.0687 found: 168.0695

N-tert-Butyl-2-(2,2-dicyano-3,5-diphenyl-cyclopent-3-enyl)-acetamide (7c)

A mixture of Passerini adduct 1c (200 mg, 1 eq), malonitrile derivative 6 (1 eq), cesium carbonate (1.2 eq) and tetrakis(triphenylphosphine)palladium (0.05 eq) in 1.3 mL of toluene was stirred at 50°C during 30min. Then the crude was heated under micro-wave at 120°C during 30min. The crude was purified by silica gel column chromatography with a gradient of Et$_2$O in EP (20:80 to 30:70), to afford 84 mg of pale yellow solid (30% yield). 

**CCM** Rf (50/50 Et$_2$O/EP) = 0.35; Mp 77 – 78°C; $^1$H-NMR (δ, ppm) (CDCl$_3$, 400 MHz) 7.57 (m, 5H), 5.48 (br s, 1H), 3.77 (d, J=7.2 Hz, 1H), 3.41 (qd, J=7.2 Hz, 1H), 2.61 (d, J=7.2 Hz, 2H), 1.26 (s, 9H); $^{13}$C-NMR (δ, ppm) (CDCl$_3$, 100.6 MHz): 166.4 (Cq), 138.0 (Cq), 136.7 (Cq), 135.5 (CH), 129.8 (Cq), 128.5 (CH), 128.2 (2CH), 128.0 (2CH), 127.1 (CH), 126.9 (2CH), 125.3 (2CH), 113.4 (Cq), 112.4 (Cq), 54.8 (CH), 54.2 (CH), 50.8 (Cq), 44.0 (Cq), 36.7 (CH$_3$), 27.6 (3CH$_3$); IR (υ, cm$^{-1}$) 3374, 2965, 1732, 1650, 1532, 1494, 1454, 1363, 1263, 1219,
N-(4-Chloro-benzyl)-2-(2,2-dicyano-3,5-diphenyl-cyclopent-3-enyl)-acetamide (7d)

A mixture of Passerini adduct 1d (100 mg, 1 eq), malonitrile derivative 6 (1 eq), cesium carbonate (1.2 eq) and tetrakis(triphenylphosphine)palladium (0.05 eq) in 1.3 mL of toluene was stirred at 50°C during 30min. The crude was purified by silica gel column chromatography with a gradient of AcOEt in EP (20:80 to 40:60), to afford 69 mg of green solid (62% yield). CCM Rf (40/60 AcOEt/EP) = 0.59; Mp 153 – 155°C; 1H-NMR (δ, ppm) (CDCl₃, 400 MHz) 7.65 (d, J=7.6 Hz, 2H), 7.45 (m, 4H), 7.39 (m, 4H), 7.29 (d, J=8.4 Hz, 2H), 7.20 (d, J=8.4 Hz, 2H), 6.42 (s, 1H), 5.90 (br s, 1H), 4.40 (d, J=5.6 Hz, 2H), 3.89 (dd, J=9.2, 2.0 Hz, 1H), 3.49 (dt, J=9.2, 5.2 Hz, 2H), 2.80 (dq, J=15.2, 9.6 Hz, 2H); 13C-NMR (δ, ppm) (CDCl₃, 100.6 MHz) 168.5 (Cq), 139.0 (Cq), 137.8 (Cq), 136.5 (CH), 136.3 (Cq), 133.4 (Cq), 130.8 (Cq), 129.7 (CH), 129.4 (2CH), 129.3 (2CH), 129.1 (2CH), 129.2 (2CH), 128.3 (CH), 128.0 (2CH), 114.6 (Cq), 113.3 (Cq), 55.7 (CH), 55.2 (CH), 45.3 (Cq), 43.1 (CH₂), 28.7 (3CH₃); IR (υ, cm⁻¹) 3290, 2965, 2925, 1667, 1629, 1540, 1453, 1391, 1362, 1265, 1226, 1090, 1014; HRMS (EI) Calcd. for C₂₈H₂₂ClN₃O: 451.1451 found: 451.1459

7,7-Dicyano-4,6-diphenyl-hepta-2,6-dienoic acid tert-butylamide (8c)

A mixture of Passerini adduct 1c (100 mg, 1 eq), malonitrile derivative 6 (1 eq), cesium carbonate (1.2 eq) and tetrakis(triphenylphosphine)palladium (0.05 eq) in 1.3 mL of toluene was stirred at 50°C during 30min. The crude was purified by silica gel column chromatography with a gradient of Et₂O in EP (20:80 to 50:50), to afford 82 mg of yellow solid (59% yield). CCM Rf (70/30 Et₂O/EP) = 0.32 Mp 75 – 77°C; 1H-NMR (δ, ppm) (CDCl₃, 400 MHz) 7.54 (d, J=7.2 Hz, 1H), 7.48 (t, J=6.8 Hz, 2H), 7.29 (m, 5H), 6.99 (d, J=7.6 Hz, 2H), 6.84 (dd, J=15.2, 6.0 Hz, 1H), 5.54 (d, J=15.2 Hz, 1H), 5.23 (br s, 1H), 3.48 (dd, J=14.8, 11.2 Hz, 1H), 3.40 (m, 2H), 1.35 (s, 9H); 13C-NMR (δ, ppm) (CDCl₃, 100.6 MHz) 177.0 (Cq), 164.2 (Cq), 143.06 (CH), 138.6 (Cq), 134.3 (Cq), 132.2 (CH), 129.3 (2CH), 129.0 (2CH), 127.9 (2CH), 127.6 (2CH), 125.9 (CH), 112.5 (Cq), 112.4 (Cq), 86.5 (Cq), 51.5 (Cq), 46.8 (CH), 42.6 (CH₂), 28.7 (3CH₃); IR (υ, cm⁻¹) 3290, 2965, 2925, 2228, 1667, 1629, 1540, 1453, 1391, 1362, 1265, 1226, 1077; HRMS (EI) Calcd. for C₂₈H₂₄ClN₃O: 451.1451 found: 451.1459
1d

ppm (H1)

1d

ppm (C1)
**8c**

[Chemical structure and related 2D NMR spectra]