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Supporting Information

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The First Organocatalytic Asymmetric Domino Knoevenagel–Diels-Alder Reactions: A Bioorganic Approach to the Diastereospecific and Enantioselective Construction of Highly Substituted Spiro[5,5]undecane-1,5,9-triones.

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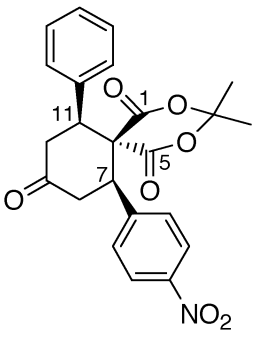
General Methods. The ^{1}H NMR and ^{13}C NMR spectra were recorded at 400 MHz and 100 MHz, respectively. The chemical shifts are reported in ppm downfield to TMS (δ=0) for ^{1}H NMR and relative to the central $CDCl_3$ resonance (δ=77.0) for ^{13}C NMR. The coupling constants *J* are given in Hz. Flash chromatography (FC) was performed using silica gel Merck 60 (particle size 0.040-0.063 mm). Optical rotations were recorded on a Perkin Elemer 241 Polarimeter (λ = 589 nm, 1 dm cell). High resolution mass spectra were recorded on an IonSpec FTMS mass spectrometer with a DHB-matrix. Electrospray ionization (ESI) mass spectrometry were performed on an API 100 Perkin-Elmer SCIEX single quadrupole mass spectrometer. The enantiomeric excess (*ee*) of the products were determined by HPLC using Daciel chiralcel OD-H or Daciel chiralpak AS or Daciel chiralpak AD columns with *i*-PrOH/hexane as eluent. HPLC was carried out using a Hitachi organizer consisting of a D-2500 Chromato-Integrator, a L-4000 UV-Detector, and a L-6200A Intelligent Pump. For thin-layer chromatography (TLC), silica gel plates Merck 60 F254 were used and compounds were visualized by irradiation with UV light and/or by treatment with a solution of *p*-anisaldehyde (23 mL), conc. H_2SO_4 (35 mL), acetic acid (10 mL), and ethanol (900 mL) followed by heating.

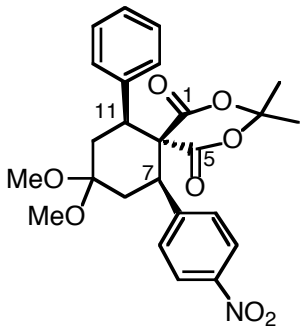
Materials. All solvents and commercially available chemicals were used as received. **General Experimental Procedure for the Preparation of Highly Substituted Spiro[5,5]undecane-1,5,9-triones by using Amino Acid Catalyzed ATCDA Reaction:**

In an ordinary glass vial equipped with a magnetic stirring bar, to 0.5 mmol of the aldehyde and 0.5 mmol of Meldrum's acid was added 1.0 mL of solvent, and then the catalyst amino acid (0.1 mmol) was added and the reaction mixture was stirred at ambient temperature for 10 to 15 minutes. To the reaction mixture 1.0 mmol of enone was added and stirred at ambient temperature for the time indicated in table. The crude reaction mixture was treated with saturated aqueous ammonium chloride solution, the layers were separated, and the organic layer was extracted three to four times with dichloromethane, dried with anhydrous Na_2SO_4, and evaporated. The pure Diels-Alder products were obtained by flash column chromatography (silica gel, mixture of hexane/ethyl acetate).

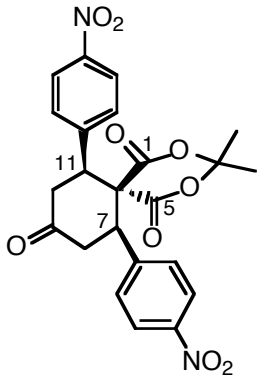


(7*R*,11*S*)-3,3-Dimethyl-7-(4-nitrophenyl)-11-phenyl-2,4-dioxa-spiro[5,5]undecane-1,5,9-trione (5aa). Purified by FC using EtOAc/hexane and isolated as a white solid. A single recrystalization in $CHCl_3$/hexane increased the optical purity to 99% *ee*. The ee was determined by chiral-phase HPLC using a Daicel Chiralcell OD-H column (hexane/*i*-PrOH = 85:15, flow rate 1.0 mL/min, λ = 254 nm), t_R = 18.90 min (major), t_R = 21.27 min (minor) (or) determined by chiral-phase HPLC using a Daicel Chiralpak AS column (hexane/*i*-PrOH = 55:45, flow rate 1.0 mL/min, λ = 266 nm), t_R = 34.11 min (major), t_R = 79.82 min (minor). $[\alpha]^{20}_D$= +0.5^0 (*c* = 2.0 g/100 mL, $CHCl_3$, 91% ee); ^{1}H NMR ($CDCl_3$) δ 8.18 (2H, td, *J* = 8.8, 2.0 Hz), 7.41 (2H, td, *J* = 8.8, 2.0 Hz) [*p*-NO_2-Ar-*H*]; 7.35-7.25 (5H, m, Ph-*H*); 4.09 (1H, dd, *J* = 14.4, 4.4 Hz, H-7); 3.99 (1H, dd, *J* = 14.4, 4.4 Hz, H-11); 3.68 (2H, dt, *J* = 14.8, 5.2 Hz, H-8); 2.63 (2H, ddt, *J* = 15.0, 4.0, 1.2 Hz, H-10); 0.62 (3H, s), 0.47 (3H, s) [2 x *tert*-C*H*$_3$]; ^{13}C NMR ($CDCl_3$) δ 206.1 (C, C=O), 167.7 (C, O=C-O), 164.9 (C, O=C-O), 147.8 (C), 144.1 (C), 136.6 (C), 129.6 (2 x CH), 129.4 (2 x CH), 128.99 (CH), 128.4 (2 x CH), 124.2 (2 x CH), 106.6 (C, O-C-O), 60.0 (C, C-6), 50.0 (CH), 49.7 (CH), 42.7 (CH_2), 42.4 (CH_2), 28.8 (CH_3), 28.0 (CH_3); HRMS (MALDI-FTMS) m/z 446.1209 (M + Na^+), calcd for $C_{23}H_{21}O_7N\ Na^+$ 446.121.

(7*R*,11*S*)-3,3-Dimethyl-9,9-dimethoxy-7-(4-nitrophenyl)-11-phenyl-2,4-dioxa-spiro[5,5]undecane-1,5-dione (7aa). Purified by FC using EtOAc/hexane and isolated as an oil and did not check the ee. ^{1}H NMR ($CDCl_3$) δ 8.13 (2H, br d, *J* = 8.8 Hz), 7.39 (2H, br d, *J* = 8.8 Hz) [*p*-NO_2-Ar-*H*]; 7.32 - 7.16 (5H, m, phenyl-*H*), 3.96 (1H, dd, *J* = 13.6,

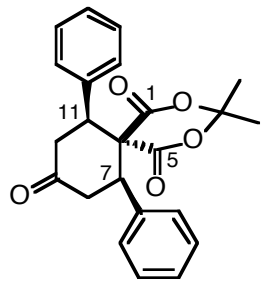


4.0 Hz), 3.82 (1H, dd, *J* = 13.6, 4.0 Hz), 3.27 (3H, s, OC*H*$_3$), 3.22 (3H, s, OC*H*$_3$), 2.78 (2H, t, *J* = 13.6 Hz), 2.16 (2H, br t, *J* = 14.0 Hz), 0.55 (3H, s, *tert*-C*H*$_3$), 0.41 (3H, s, *tert*-C*H*$_3$); ^{13}C NMR ($CDCl_3$) 168.9 (C, O=C-O), 164.8 (C, O=C-O), 147.5 (C), 146.0 (C), 138.3 (C), 129.9 (2 x CH), 129.1 (2 x CH), 128.8 (2 x CH), 128.4 (CH), 123.9 (2 x CH), 105.8 (C, O-*C*-O, C-3), 99.2 (C, O-*C*-O, C-9), 60.8 (C, C-6), 47.97 (CH_3, OCH_3), 47.90 (CH_3, OCH_3), 47.43 (CH), 47.37 (CH), 33.2 (CH_2), 33.1 (CH_2), 28.9 (CH_3), 28.0 (CH_3).



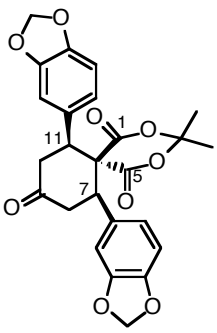
(7,11)-3,3-Dimethyl-7,11-(di 4-nitrophenyl)-2,4-dioxa-spiro[5,5]undecane-1,5,9-trione (6aa). Purified by FC using EtOAc/hexane and isolated as a white solid and it has a plane of symmetry. ^{1}H NMR ($CDCl_3$) 8.23 (4H, td, *J* = 8.8, 2.0 Hz), 7.44 (4H, td, *J* = 8.8, 2.0 Hz) [Aromatic-*H*]; 4.14 (2H, dd, *J* = 14.4, 4.0 Hz), 3.72 (2H, t, *J* = 14.8 Hz), 2.70 (2H, dd, *J* = 14.8, 4.0 Hz), 0.63 (6H, s, 2 x *tert*-C*H*$_3$); ^{13}C NMR ($CDCl_3$) 204.6 (C, C=O), 167.3 (C, O=C-O), 164.6 (C, O=C-O), 148.1 (2 x C), 143.5 (2 x C), 129.7 (4 x CH), 124.4 (4 x CH), 106.8 (C, O-C-O), 59.5 (C, C-6), 49.8 (2 x CH), 42.3 (2 x CH_2), 28.7 (2 x CH_3); ESI m/z 467 (M – H), calcd for $C_{23}H_{20}O_9N_2$ 467.1096.

(7,11)-3,3-Dimethyl-7,11-diphenyl-2,4-dioxa-spiro[5,5]undecane-1,5,9-trione



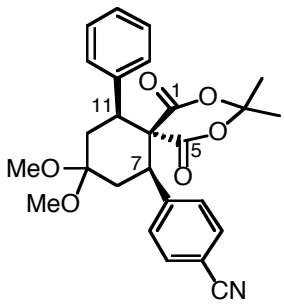
(5ac). Purified by FC using EtOAc/hexane and isolated as light yellow colored solid. Note the product contains a plane of symmetry. ^{1}H NMR ($CDCl_3$) 7.33 – 7.10 (10H, m, Ph-*H*), 3.96 (2H, dd, *J* = 14.4, 4.4 Hz, H-7 & 11), 3.66 (2H, t, *J* = 14.4 Hz), 2.58 (2H, ddd, *J* = 14.4, 4.4, 0.8 Hz), 0.49 (6H, s, 2 x *tert*-CH_3); ^{13}C NMR ($CDCl_3$) 207.4 (C, C=O), 168.0 (C, O=C-O), 165.1 (C, O-C=O), 136.9 (2 x C), 129.1 (4 x CH), 128.6 (2 x CH), 128.3 (4 x CH), 106.2 (C, O-*C*-O), 60.4 (C, C-6), 49.9 (2 x CH), 42.7 (2 x CH_2), 28.2 (2 x CH_3); HRMS (MALDI-FTMS) m/z 401.1352 (M + Na^+), calcd for $C_{23}H_{22}O_5$ Na^+ 401.1359.

(7,11)-3,3-Dimethyl-7,11-bis-benzo[1,3]dioxol-5-yl-2,4-dioxa-spiro[5,5]undecane-1,5,9-trione (5bd). Purified by FC using EtOAc/hexane and isolated as light yellow



colored solid. Note the product contains a plane of symmetry. ^{1}H NMR ($CDCl_3$) □ 6.76 (2H, d, *J* = 8.0 Hz, Ph-*H*), 6.71 (2H, s, Ph-*H*), 6.70 (2H, d, J = 8.4 Hz, Ph-*H*), 5.94 (4H, s, -OC*H*$_2$O-), 3.89 (2H, dd, *J* = 14.0, 4.4 Hz, H-7 & 11), 3.58 (2H, t, *J* = 14.4 Hz), 2.58 (2H, dd, *J* = 14.8, 4.4 Hz), 0.80 (6H, s, 2 x *tert*-CH_3); ^{13}C NMR ($CDCl_3$) □ 207.1 (C, C=O), 168.1 (C, O=C-O), 165.2 (C, O-C=O), 148.0 (2 x C), 147.5 (2 x C), 130.7 (2 x C), 121.9 (2 x CH), 108.6 (2 x CH), 108.58 (2 x CH), 106.2 (C, O-*C*-O), 101.2 (2 x CH_2, O*C*H_2O), 60.5 (C, C-6), 49.5 (2 x CH), 43.1 (2 x CH_2), 28.5 (2 x CH_3); HRMS (MALDI-FTMS) m/z 489.1155 (M + Na^+), calcd for $C_{25}H_{22}O_9$ Na^+ 489.1156.

(7*R*,11*S*)-4-(3,3-Dimethyl-1,5,9-trioxo-11-phenyl-2,4-dioxa-spiro[5,5]undec-7-yl)-benzonitrile (5ab). Purified by FC using EtOAc/hexane and isolated as a white solid. The ee was determined by chiral-phase HPLC using a Daicel Chiralcell OD-H column (hexane/*i*-PrOH = 85:15, flow rate 1.0 mL/min, □ = 254 nm), t_R = 15.43 min (major), t_R = 18.76 min (minor). [□]$^{20}_D$= +0.2^0 (*c* = 2.0 g/100 mL, $CHCl_3$, 84% ee); ^{1}H NMR ($CDCl_3$) □ 7.62 (2H, td, *J* = 8.4, 2.0 Hz), 7.34 (2H, br d, *J* = 8.4 Hz), 7.34 – 7.15 (5H, m, Ph-*H*), 4.03 (1H, dd, *J* = 14.4, 4.4 Hz, H-7), 3.98 (1H, dd, *J* = 14.4, 4.4 Hz, H-11), 3.66 (2H, td, *J* = 11.6, 14.4 Hz), 2.62 (2H, ddt, *J* = 16.0, 4.4, 1.2 Hz), 0.62 (3H, s, *tert*-CH_3), 0.48 (3H, s, *tert*-CH_3); ^{13}C NMR ($CDCl_3$) □ 206.3 (C, C=O), 167.8 (C, O-C=O), 164.9 (C, O-C=O), 142.2 (C), 136.6 (C), 132.9 (2 x CH), 129.42 (2 x CH), 129.40 (2 x CH), 128.99 (CH), 128.47 (2 x CH), 117.9 (C), 112.7 (C, CN), 106.6 (C, O-*C*-O), 60.1 (C, C-6), 50.0 (CH), 49.99 (CH), 42.7 (CH_2), 42.3 (CH_2), 28.7 (CH_3), 28.1 (CH_3); ESI m/z 402 (M □ H), calcd for $C_{24}H_{20}O_5N$ 402.1347; HRMS (MALDI-TOF) m/z 426 (M + Na^+), calcd for $C_{24}H_{21}O_5N$ Na^+ 426.1312.



(7*R*,11*S*)-4-(3,3-Dimethyl-9,9-dimethoxy-1,5-dioxo-11-phenyl-2,4-dioxa-spiro[5,5]undec-7-yl)-benzonitrile (7ab). ^{1}H NMR ($CDCl_3$) □ 7.60 (2H, td, *J* = 8.8, 2.0 Hz), 7.35 (2H, td, *J* = 8.8, 2.0 Hz), 7.34 – 7.18 (5H, m, Ph-*H*), 3.93 (1H, dd, *J* = 13.6,

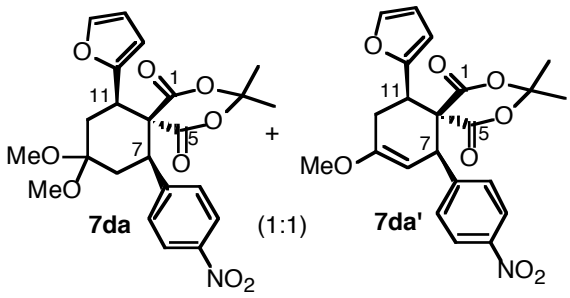
3.6 Hz), 3.84 (1H, dd, *J* = 13.6, 3.6 Hz), 3.30 (3H, s, OCH_3), 3.25 (3H, s, OCH_3), 2.79 (2H, td, *J* = 6.4, 13.6 Hz), 2.18 (2H, ddt, *J* = 13.6, 3.6, 2.0 Hz), 0.58 (3H, s, *tert*-CH_3), 0.45 (3H, s, *tert*-CH_3).

(7*R*,11*S*)-3,3-Dimethyl-7-(4-nitrophenyl)-11-(napthalen-1-yl)-2,4-dioxa-spiro[5,5]undecane-1,5,9-trione (5ca). Purified by FC using EtOAc/hexane and isolated as white solid. The ee was determined by chiral-phase HPLC using a Daicel Chiralcell OD-H column (hexane/*i*-PrOH = 85:15, flow rate 1.0 mL/min, □ = 254 nm), t_R = 45.12 min (major), t_R = 102.80 min (minor). $[\square]^{20}_D$= +29.07^0 (*c* = 1.4 g/100 mL, $CHCl_3$, 99% ee); ^{1}H NMR ($CDCl_3$) □ 8.21 (2H, td, *J* = 8.8, 2.0 Hz), 8.15 (1H, br d, *J* = 8.8 Hz), 7.83 (2H, ddd, *J* = 8.0, 3.6, 1.2 Hz), 7.64 – 7.28 (4H, m), 7.49 (2H, td, *J* = 9.2, 2.4 Hz), 4.99 (1H, dd, *J* = 14.0, 4.0 Hz), 4.30 (1H, dd, *J* = 14.0, 4.4 Hz), 3.85 (1H, t, *J* = 14.4 Hz), 3.79 (1H, t, *J* = 14.8 Hz), 2.73 (2H, dd, *J* = 15.2, 4.8 Hz), 0.59 (3H, s, *tert*-CH_3), 0.43 (3H, s, *tert*-CH_3); ^{13}C NMR ($CDCl_3$) □ 206.2 (C, C=O), 167.3 (C, O-C=O), 165.4 (C, O-C=O), 147.8 (C), 144.2 (C), 134.0 (C), 133.4 (C), 130.6 (C), 129.9 (2 x CH), 129.6 (CH), 128.8 (CH), 127.1 (CH), 126.5 (CH), 125.4 (CH), 125.2 (CH), 124.2 (2 x CH), 122.8 (CH), 106.6 (C, O-*C*-O), 59.2 (C, C-6), 50.0 (CH), 44.6 (CH_2), 43.3 (CH), 42.7 (CH_2), 29.1 (CH_3), 27.9 (CH_3); ESI m/z 472 (M □ H), calcd for $C_{27}H_{23}O_7N$ 472.1402.

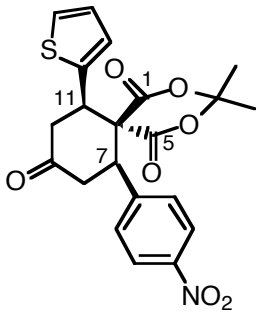
(7*R*,11*R*)-3,3-Dimethyl-7-(4-nitrophenyl)-11-(furan-2-yl)-2,4-dioxa-spiro[5,5]undecane-1,5,9-trione (5da). Purified by FC using EtOAc/hexane and isolated as a white solid. The ee was determined by chiral-phase HPLC using a Daicel Chiralcell OD-H column (hexane/*i*-PrOH = 98:2, flow rate 0.2 mL/min, □ = 254 nm), t_R = 113.74 min (minor), t_R = 120.62 min (major). $[\square]^{20}_D$= □1.54^0 (*c* = 2.33 g/100 mL, $CHCl_3$, 88% ee); ^{1}H NMR ($CDCl_3$) □ 8.23 (2H, td, *J* = 9.2, 2.4 Hz), 7.45 (2H, td, *J* = 8.8, 2.4 Hz), 7.38 (1H, dd, *J* = 2.0, 0.8 Hz), 6.35 (1H, dd, *J* = 3.2, 1.6 Hz), 6.26 (1H, d, *J* = 3.2 Hz), 4.20 (1H, dd, *J* = 14.4, 4.4 Hz), 4.07 (1H, dd, *J* = 14.4, 4.4 Hz), 3.64 (2H, dt, *J* = 14.8, 4.0 Hz), 2.72 (1H, ddd, *J* = 15.6, 4.8, 1.6 Hz), 2.65 (1H, ddd, *J* = 15.6, 4.4, 1.6 Hz), 0.98 (3H, s, *tert*-CH_3), 0.75 (3H, s, *tert*-CH_3); ^{13}C NMR ($CDCl_3$) □ 205.1 (C, C=O), 167.7 (C, O-C=O), 164.4 (C, O-

C=O), 150.3 (C), 147.9 (C), 143.8 (C), 142.9 (CH), 129.6 (2 x CH), 124.2 (2 x CH), 110.9 (CH), 109.2 (CH), 106.5 (C, O-*C*-O), 58.2 (C, C-6), 49.1 (CH), 43.7 (CH), 42.2 (CH_2), 41.2 (CH_2), 28.6 (CH_3), 28.4 (CH_3); ESI m/z 412 (M □ H), calcd for $C_{21}H_{19}O_8N$ 412.1038.

(7*R*,11*R*)-3,3-Dimethyl-9,9-dimethoxy-7-(4-nitrophenyl)-11-(furan-2-yl)-2,4-dioxa-spiro[5,5]undecane-1,5-dione (7da) and (7*R*,11*R*)-3,3-Dimethyl-9-methoxy-7-(4-nitrophenyl)-11-(furan-2-yl)-2,4-dioxa-spiro[5,5]undec-8-ene-1,5-dione (7da').



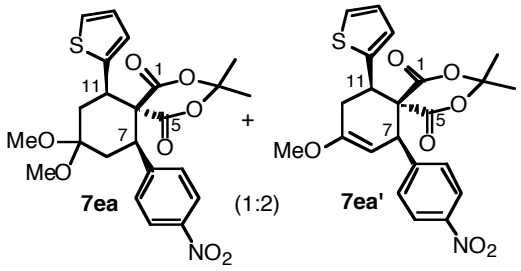
Purified by FC using EtOAc/hexane and isolated as oil with 1:1 mixture of **7da** and **7da'**. ^{1}H NMR ($CDCl_3$) for the compound **7da**: □ 8.18 (2H, td, *J* = 8.8, 2.0 Hz), 7.42 (2H, td, *J* = 8.8, 2.0 Hz), 7.33 (1H, dd, *J* = 2.0, 0.8 Hz), 6.30 (1H, dd, *J* = 3.2, 2.0 Hz), 6.20 (1H, br d, *J* = 3.2 Hz), 4.01 (1H, dd, *J* = 14.0, 3.6 Hz), 3.92 (1H, dd, *J* = 14.0, 3.6 Hz), 3.30 (3H, s, OC*H*$_3$), 3.24 (3H, s, OC*H*$_3$), 2.76 (1H, t, J = 14.0 Hz), 2.71 (1H, t, J = 14.0 Hz), 2.25 (1H, ddd, *J* = 14.0, 3.6, 2.4 Hz), 2.14 (1H, ddd, *J* = 13.6, 3.6, 2.4 Hz), 0.75 (3H, s, *tert*-CH_3), 0.64 (3H, s, *tert*-CH_3);); ^{1}H NMR ($CDCl_3$) for the compound **7da'**: □ 8.19 (2H, td, *J* = 8.8, 2.0 Hz), 7.45 (2H, td, *J* = 8.8, 2.0 Hz), 7.33 (1H, dd, *J* = 2.0, 0.8 Hz), 6.34 (1H, dd, *J* = 3.6, 2.4 Hz), 6.28 (1H, br d, *J* = 2.4 Hz), 4.81 (1H, br s, olefinic-*H*), 4.69 (1H, br s, H-7), 4.01 (1H, dd, *J* = 14.0, 3.6 Hz), 3.66 (3H, s, OC*H*$_3$), 3.17 (1H, ddt, *J* = 16.8, 3.2, 1.6 Hz), 2.42 (1H, dd, *J* = 16.8, 5.6 Hz), 0.99 (3H, s, *tert*-CH_3), 0.93 (3H, s, *tert*-CH_3); ESI m/z 458 (M □ H), calcd for $C_{23}H_{25}O_9N$ 458.1456.



(7*R*,11*R*)-3,3-Dimethyl-7-(4-nitrophenyl)-11-(thiophen-2-yl)-2,4-dioxa-spiro[5,5]undecane-1,5,9-trione (5ea). Purified by FC using EtOAc/hexane and isolated as white solid. The ee was determined by chiral-phase HPLC using a Daicel Chiralcell OD-H column (hexane/*i*-PrOH = 99:1, flow rate 0.15 mL/min, □ = 254 nm), t_R = 179.92 min (minor), t_R = 187.02 min (major). [□]$^{20}_D$= □2.46^0 (*c* = 1.75 g/100 mL, $CHCl_3$, 99% ee); ^{1}H NMR ($CDCl_3$) □ 8.19 (2H, td, *J* = 8.8, 2.0 Hz), 7.40 (2H, td, *J* = 8.8, 2.0 Hz), 7.22 (1H, dd, *J* = 4.8, 1.6 Hz), 7.00 – 6.90 (2H, m), 4.36 (1H, dd, *J* = 14.0, 4.4 Hz), 4.04 (1H, dd, *J* = 14.0,

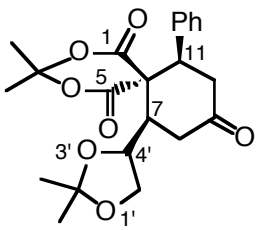
4.4 Hz), 3.63 (1H, t, *J* = 14.8 Hz), 3.60 (1H, t, *J* = 14.8 Hz), 2.80 (1H, ddd, *J* = 15.2, 4.8, 1.2 Hz), 2.61 (1H, ddd, *J* = 15.2, 4.4, 1.2 Hz), 0.69 (6H, s, 2 x *tert*-CH_3); ^{13}C NMR ($CDCl_3$) 204.8 (C, C=O), 167.9 (C, O-C=O), 164.8 (C, O-C=O), 147.8 (C), 143.7 (C), 139.6 (C), 129.4 (2 x CH), 127.4 (CH), 127.3 (CH), 125.8 (CH), 124.2 (2 x CH), 106.7 (C, O-*C*-O), 60.5 (C, C-6), 49.6 (CH), 44.9 (CH), 44.2 (CH_2), 42.0 (CH_2), 28.6 (CH_3), 28.4 (CH_3); HRMS (MALDI-FTMS) m/z 452.0787 (M + Na^+), calcd for $C_{21}H_{19}O_7NS$ Na^+ 452.0774.

(7*R*,11*R*)-3,3-Dimethyl-9,9-dimethoxy-7-(4-nitrophenyl)-11-(thiophen-2-yl)-2,4-dioxa-spiro[5,5]undecane-1,5-dione (7ea) and (7*R*,11*R*)-3,3-Dimethyl-9-methoxy-7-(4-nitrophenyl)-11-(thiophen-2-yl)-2,4-dioxa-spiro[5,5]undec-8-ene-1,5-dione (7ea').



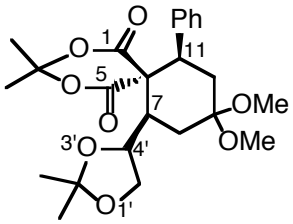
Purified by FC using EtOAc/hexane and isolated as oil with 1:2 mixture of **7ea** and **7ea'**. ^{1}H NMR ($CDCl_3$) for the minor compound **7ea**: 8.17 (2H, td, *J* = 8.8, 2.0 Hz), 7.40 (2H, td, *J* = 8.8, 2.0 Hz), 7.18 (1H, dd, *J* = 4.4, 1.6 Hz), 6.94 (2H, m), 4.19 (1H, dd, *J* = 14.0, 4.4 Hz), 3.91 (1H, dd, *J* = 14.0, 4.4 Hz), 3.30 (3H, s, OCH_3), 3.25 (3H, s, OCH_3), 2.77 (1H, t, *J* = 13.6 Hz), 2.75 (1H, t, *J* = 13.6 Hz), 2.35 (1H, ddd, *J* = 13.6, 3.6, 2.0 Hz), 2.15 (1H, ddd, *J* = 13.6, 3.6, 2.0 Hz), 0.66 (3H, s, *tert*-CH_3), 0.64 (3H, s, *tert*-CH_3); ^{1}H NMR ($CDCl_3$) for the major compound **7ea'**: 8.19 (2H, td, *J* = 8.8, 2.0 Hz), 7.44 (2H, td, *J* = 8.8, 2.0 Hz), 7.21 (1H, dd, *J* = 5.2, 1.2 Hz), 7.00 (1H, dd, *J* = 3.6, 0.8 Hz), 6.94 (1H, m), 5.00 (1H, s, olefinic-*H*), 4.77 (1H, s, H-7), 4.01 (1H, dd, *J* = 12.0, 5.6 Hz), 3.65 (3H, s, OCH_3), 3.15 (1H, ddt, *J* = 12.4, 4.8, 2.0 Hz), 2.43 (1H, dd, *J* = 17.2, 5.2 Hz), 0.75 (3H, s, *tert*-CH_3), 0.74 (3H, s, *tert*-CH_3).

(4'*S*,7*R*,11*R*)-3,3-Dimethyl-7-(2,2-dimethyl-[1,3]dioxolan-4-yl)-11-phenyl-2,4-dioxa-spiro[5,5]undecane-1,5,9-trione (15). Purified by FC using EtOAc/hexane and isolated as colorless oil. ^{1}H NMR ($CDCl_3$) 7.37 – 7.17 (5H, m, Ph-*H*), 4.23 (1H, ddd, *J* = 6.8, 5.2, 2.0 Hz), 4.02 (1H, dd, *J* = 9.2, 7.2 Hz), 3.80 (1H, dd, *J* = 14.0, 4.4 Hz, H-7), 3.75 (1H, dd, *J* = 8.8, 5.2 Hz), 3.59 (1H, t, *J* = 14.0 Hz), 3.32 (1H, t, *J* = 14.0 Hz), 2.82 (1H, ddd, *J* = 14.0, 4.4, 2.0 Hz, H-11), 2.59 (1H, ddd, *J* = 15.2,

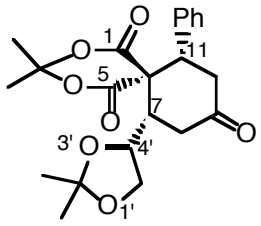


4.8, 1.6 Hz), 2.49 (1H, ddd, *J* = 15.6, 4.0, 1.2 Hz), 1.63 (3H, s, *tert*-CH_3), 1.40 (3H, s, *tert*-CH_3), 1.26 (3H, s, *tert*-CH_3), 0.65 (3H, s, *tert*-CH_3); ^{13}C NMR ($CDCl_3$) 208.3 (C, C=O), 168.9 (C, O-C=O), 164.1 (C, O-C=O), 136.7 (C), 129.2 (2 x CH), 128.8 (CH), 128.6 (2 x CH), 110.5 (C, O-*C*-O, C-2'), 106.7 (C, O-*C*-O, C-3), 74.1 (CH, C-4'), 66.2 (CH_2, C-5'), 56.5 (C, C-6), 50.1 (CH), 47.8 (CH), 42.9 (CH_2), 36.3 (CH_2), 28.9 (CH_3), 28.5 (CH_3), 25.5 (CH_3), 24.5 (CH_3); HRMS (MALDI-FTMS) m/z 425.1566 (M + Na^+), calcd for $C_{22}H_{26}O_7\ Na^+$ 425.1571.

(4'*S*,7*R*,11*R*)-3,3-Dimethyl-9,9-dimethoxy-7-(2,2-dimethyl-[1,3]dioxolan-4-yl)-11-phenyl-2,4-dioxa-spiro[5,5]undecane-1,5-dione (14). Purified by FC using EtOAc/hexane and isolated as colorless oil. ^{1}H NMR ($CDCl_3$) 7.30 – 7.13 (5H, m, Ph-*H*), 4.11 (1H, ddd, *J* = 7.2, 5.2, 2.0 Hz), 3.98 (1H, dd, *J* = 8.4, 6.8 Hz), 3.72 (1H, dd, *J* = 8.8, 5.6 Hz), 3.61 (1H, dd, *J* = 13.6, 4.0 Hz), 3.24 (3H, s, OC*H*$_3$), 3.15 (3H, s, OC*H*$_3$), 2.72 (1H, t, *J* = 13.6 Hz), 2.63 (1H, td, *J* = 13.2, 3.2 Hz, H-11), 2.34 (1H, t, *J* = 14.0 Hz), 2.06 (1H, ddd, *J* = 13.6, 3.6, 2.0 Hz), 1.99 (1H, br td, *J* = 14.0, 2.8 Hz), 1.53 (3H, s, *tert*-CH_3), 1.35 (3H, s, *tert*-CH_3), 1.20 (3H, s, *tert*-CH_3), 0.53 (3H, s, *tert*-CH_3); ^{13}C NMR ($CDCl_3$) 170.1 (C, O-C=O), 164.0 (C, O-C=O), 138.5 (C), 128.96 (2 x CH), 128.90 (2 x CH), 128.1 (CH), 110.2 (C, O-*C*-O, C-2'), 105.9 (C, O-*C*-O, C-3), 99.6 (C, O-*C*-O, C-9), 74.6 (CH, C-4'), 66.7 (CH_2, C-5'), 57.6 (C, C-6), 47.9 (CH_3, OC*H*$_3$), 47.6 (CH_3, OC*H*$_3$), 47.6 (CH), 45.8 (CH), 33.6 (CH_2), 29.0 (CH_3), 28.4 (CH_3), 26.5 (CH_2), 25.6 (CH_3), 24.5 (CH_3); ESI m/z 471 (M + Na^+), calcd for $C_{24}H_{32}O_8Na^+$ 471.1989.

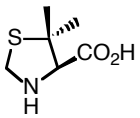
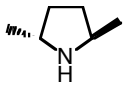
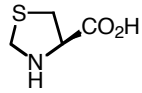
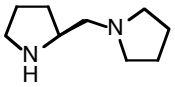
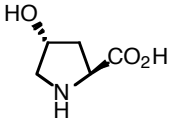
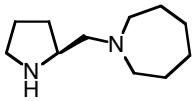
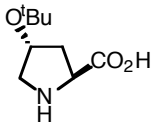
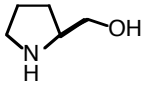
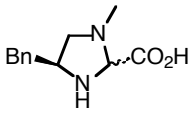
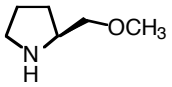
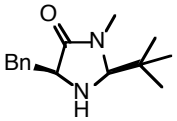
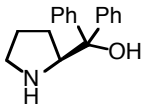
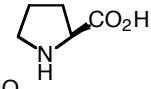
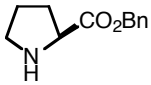
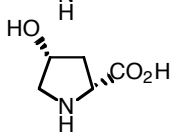
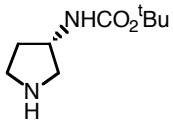
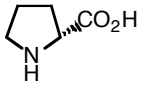
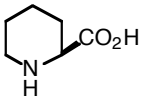


(4'*R*,7*S*,11*S*)-3,3-Dimethyl-7-(2,2-dimethyl-[1,3]dioxolan-4-yl)-11-phenyl-2,4-dioxa-spiro[5,5]undecane-1,5,9-trione. (minor ketone and not clean) Purified by FC using EtOAc/hexane and isolated as light colored yellow oil. ^{1}H NMR ($CDCl_3$) 7.36 – 7.16 (5H, m, Ph-*H*), 4.18 (1H, ddd, *J* = 6.8, 4.4, 2.0 Hz), 4.05 (1H, dd, *J* = 9.2, 7.2 Hz), 3.92 (1H, m), 3.85 (1H, dd, *J* = 9.2, 4.8 Hz), 3.20 (1H, dd, *J* = 13.2, 2.0 Hz), 2.71 (1H, ddd, *J* = 13.2, 3.2, 2.0 Hz), 2.54 (1H, t, *J* = 13.6 Hz), 2.43 (1H, ddd, *J* = 9.6, 6.0, 1.6 Hz), 2.30 (1H, dd, *J* = 14.0, 3.2 Hz), 1.58 (3H, s, *tert*-CH_3), 1.41 (3H, s, *tert*-CH_3), 1.24 (3H, s, *tert*-CH_3), 0.58 (3H, s, *tert*-CH_3).



Catalyst Screening Table:

Table 2. Structure/reactivity of amino acid effect on the direct amino acid catalyzed ATCDA reaction of *trans*-4-phenyl-3-buten-2-one **1a**, 4-nitrobenzaldehyde **2a** and Meldrum's acid **3** in methanol at 25 °C. [a]

Entry	Amine	Time [h]	Yield [%][b]		ee for **5aa** [%][c]	Entry	Amine	Time [h]	Yield [%][b]		ee for **5aa** [%][c]
			5aa	**6aa**					**5aa**	**6aa**	
1		48	14	17	□	11		72	88	trace	86
2		120	10	8	41	12		84	65	trace	89
3[d]		72	56	12	45	13		96	50	4	91
4		72	80	13	24	14		84	84	trace	76
5		96	12	17	68	15[e]		96	64	14	70
6		120	12	17	65	16		72	□	□	□
7		120	10	9	32	17		48	85	7	60
8		96	23	trace	35	18		84	70	trace	60
9		48	40	34	40	19		72	80	trace	34
10		120	7	17	60						

[a] See Supporting Information. [b] Yield refers to the column purified product. [c] Enantiomeric excesses were determined by using chiral phase HPLC. [d] Reaction was performed in THF as solvent. [e] Reaction performed at 4 °C.

Figure 3. X-ray crystal structure of spiro[5,5]undecane-1,5,9-trione (5aa).