Tandem Regioselective Rhodium-Catalyzed Hydroformylation–Enantioselective Aminocatalytic *anti*-Mannich Reaction

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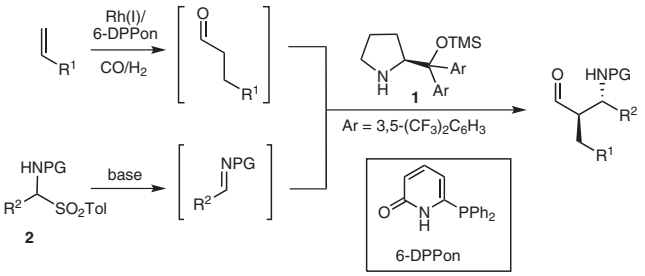
Abstract: The first tandem regioselective hydroformylation and enantioselective organocatalytic *anti*-Mannich reaction is reported. Starting from α-olefins, valuable functionalized amino acid derivatives were obtained in excellent yields and with high levels of diastereo- and enantioselectivities. The products represent valuable building blocks for biologically and pharmaceutically interesting targets.

Key words: tandem reactions, asymmetric synthesis, homogeneous catalysis, organocatalysis, hydroformylation

Functionalized α-amino acid derivatives are valuable building blocks for the synthesis of target structures of biological and medicinal interest.[1] As such, the development of methods for their preparation has drawn a lot of attention.[2–4] Among the many approaches used to achieve this goal, an elegant process is the organocatalytic Mannich reaction between enolizable aldehydes and imines.[5–7] However, enolizable aldehydes themselves are reactive substrates that may undergo side reactions such as aldol reactions and oligomerization, which can be obstructive for obtaining high yields. One strategy to avoid such undesired side reactions is to generate the aldehyde in a low stationary concentration by way of a catalytic reaction. As we have demonstrated recently, this can be efficiently achieved by generating an aldehyde in situ through the application of atom-economic hydroformylation of alkenes. By applying this strategy, we were able to develop an efficient enantioselective tandem regioselective hydroformylation and organocatalytic enantioselective aldol addition[8] as well as a tandem regioselective hydroformylation–Biginelli reaction.[9,10] We report herein on an extension of this concept with the development of the first tandem regio-, diastereo- and enantioselective hydroformylation–organocatalytic *anti*-Mannich reaction.

Among the different known methods for organocatalytic Mannich reactions, we were attracted by the *anti*-selective Mannich methodology developed by Melchiore et al.[7] Central to this method is the generation of N-carbamate-substituted imines in situ through base-initiated elimination of tolyl sulfinic acid from stable α-amidosulfones **2** (Scheme 1). An interesting aspect of this method is that *N*-Boc or *N*-Cbz protected α-amino acids are obtained directly, which allows for follow-up peptide construction.



Scheme 1 Design of a domino hydroformylation–aminocatalytic *anti*-Mannich reaction

A crucial factor for success of the envisioned tandem hydroformylation–Mannich approach was the selection of the optimal catalyst system for the hydroformylation step. First, the catalyst has to be compatible with the substrates, reagents and the organocatalyst present at the same time. Second, it has to operate under mild conditions to allow for low reaction temperatures to ensure good enantioselectivities in the organocatalytic Mannich step. Finally the enolizable aldehyde reaction partner has to be generated through hydroformylation in high chemo- and regioselectivities.

A catalyst system that has the potential to fulfill all these demands could be the self-assembling 6-diphenylphosphinopyridone/rhodium catalyst (6-DPPon see Scheme 1) developed in our group.[11] As demonstrated recently, this catalyst allows for hydroformylation at room temperature and ambient pressure in the presence of a large number of functional groups, and even water can be applied as the solvent in the presence of catalytic amounts of a suitable surfactant.[12,13] Notably, this catalyst system has displayed hydroformylation activity in an asymmetric tandem hydroformylation–aldol reaction at temperatures as low as 4 °C.[8]

Initial experiments applying the typical organocatalytic conditions developed previously[7] in the presence of 1-octene, synthesis gas, 0.5 mol% rhodium catalyst and amidosulfone **2a** as the imine precursor, gave only moderate yields under ambient pressure and at room temperature. However, increasing the rhodium catalyst loading to 2.7 mol% furnished the tandem product in good yield (Table 1, entry 1). However, a catalyst loading of 2.7 mol% rhodium is unusually high for our 6-DPPon catalyst, which is

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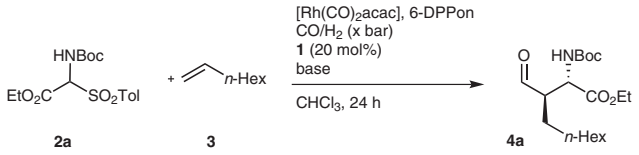
significantly more active under standard hydroformylation conditions.[11,12] Clearly, one of the reagents in this tandem process retarded the hydroformylation catalyst activity. We questioned whether this was due to the excess of the fluoride salt (5 equiv) required to generate the imine. However, reducing the amount of KF to two equivalents did not give a better result (entry 2). Next, a screening of alternative bases was undertaken and, interestingly, dipotassium phosphate was found to be most efficient (entries 3–6). With this new base, which was capable of initiating the necessary sulfinic acid elimination, it was possible to lower the rhodium catalyst loading to 0.25 mol% when the pressure was raised to 20 bar and the reaction temperature was increased to 45 °C, affording **4a** in quantitative yield and in excellent selectivity (Table 1, entry 9).

Table 1 Optimization of the Tandem Reaction Conditions with **2a** and **3**[a]



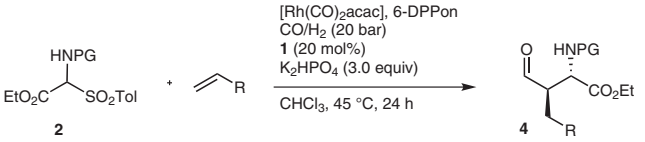
2a **3** **4a**

Entry	Base (equiv)	Pressure (bar)	Temp (°C)	Yield (%)[b]	dr[c]
1[d]	KF (5.0)	1	r.t.	90	98:2
2[d]	KF (2.0)	1	r.t.	58	>99:1
3[d]	$KHCO_3$ (2.0)	1	r.t.	35	90:10
4[d]	*i*-Pr_2NEt (2.0)	1	r.t.	44	84:14
5[d]	K_2HPO_4 (2.0)	1	r.t.	72	97:3
6[d]	K_2HPO_4 (5.0)	1	r.t.	86	97:3
7[e]	K_2HPO_4 (5.0)	20	r.t.	67	98:2
8[e]	K_2HPO_4 (5.0)	20	50	99	95:5
9[f]	K_2HPO_4 (3.0)	20	45	99	98:2

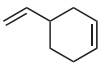
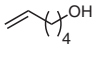
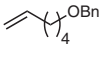
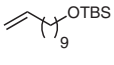
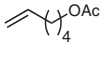
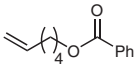
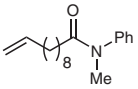
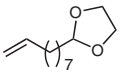
[a] 1-Octene was used as standard olefin.
[b] Yield was determined by ^1H NMR spectroscopic analysis with 1,3,5-trimethoxybenzene as internal standard.
[c] Determined by ^1H NMR spectroscopic analysis of the crude mixture.
[d] Reaction conditions: Rh-catalyst (2.7 mol%; ratio [Rh]/L, 1:5), 1-octene (4.0 equiv).
[e] Reaction conditions: Rh-catalyst (0.5 mol%; ratio [Rh]/L, 1:5), 1-octene (2.0 equiv).
[f] Reaction conditions: Rh-catalyst (0.25 mol%; ratio [Rh]/L, 1:5), 1-octene (1.5 equiv).

With the optimal reaction conditions in hand, the scope and limitations of this new tandem reaction were evaluated. Linear olefins gave excellent yields and very good selectivities (Table 2). For the N-protecting group, the Boc group as well as the more unusual Cbz group in aminocatalytic Mannich reactions proved suitable (Table 2, entries 1 and 2).[9,10] α-Branched olefins gave slightly lower yields, however, the stereoselectivity remained high (Table 2, entries 3 and 4). Many functional groups such as unprotected hydroxyl groups (Table 2, entry 5), benzyl- and TBS-protected hydroxyl groups (Table 2, entries 6 and 7), acetates or benzoates (Table 2, entries 8 and 9), as well as amides (Table 2, entry 10) and acetals (Table 2, entry 11) were tolerated and furnished the corresponding products in high yields and very good selectivities. By employing a diolefin substrate, bis(α-amino acid β-formyl), product **4l** was obtained in a bidirectional tandem reaction in high yields (Table 2, entry 12). An internal alkene was inert under these reaction conditions (Table 2, entry 4).

Table 2 Scope of the Tandem Reaction of **2a** (PG = Boc) or **2b** (PG = Cbz) with **3**[a]



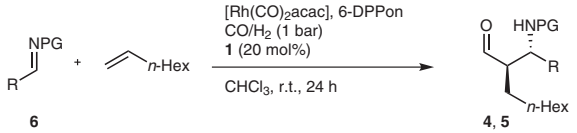
2 **4**

Entry	Olefin	PG	4	Yield (%)[b]	dr[c]	ee (%)[d]
1	*n*-Hex	Boc	**4a**	97	92:8	97
2[e]	*n*-Hex	Cbz	**4b**	98	91:9	99
3[e]	*t*-Bu	Boc	**4c**	70	95:5	>99
4		Cbz	**4d**	88	82:18	94
5[e]		Boc	**4e**	83	92:8	92
6		Boc	**4f**	85	92:8	94
7[e]		Cbz	**4g**	92	91:9	93
8		Boc	**4h**	98	93:7	89
9[e]		Boc	**4i**	76	96:4	93
10		Boc	**4j**	96	96:4	99
11		Boc	**4k**	85	94:6	93
12[f]		Boc	**4l**	84	93:7	n.d.

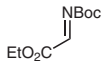
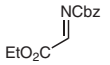
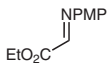
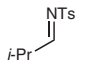
[a] Reaction conditions (0.24 mmol scale): olefin (1.5 equiv), Rh catalyst (0.25 mol%; ratio [Rh]/L, 1:5).
[b] Isolated yield.
[c] Determined by ^1H NMR spectroscopic analysis of the crude mixture.
[d] Determined by chiral HPLC analysis, for details see the Supporting Information; n.d. = not determined.
[e] Rh catalyst (0.5 mol%; ratio [Rh]/L, 1:5).
[f] Reaction carried out with olefin (0.65 equiv).

While the efficiency of a new method in terms of low catalyst loadings is certainly an important factor, of similar importance is the aspect of practicality. Along this line, we wanted to develop a tandem hydroformylation–Mannich protocol that would allow for operation at room temperature and at ambient pressure (RTAP) avoiding the need for high-pressure autoclave equipment.[11] Indeed, after some experimentation, this goal could be reached. Optimal conditions were found to require 2.5 mol% hydroformylation catalyst, 20 mol% chiral pyrrolidine catalyst **1**, and an excess of five equivalents of KF to generate the imine. Under these conditions, good yields and excellent selectivities were noted (Table 3, entries 1 and 2). Furthermore, when the known *N*-PMP- and *N*-tosyl-substituted imines were prepared and subjected to these RTAP conditions the corresponding tandem-products **5** were formed, albeit in slightly lower yields and stereoselectivities (Table 3, entries 3 and 4).

Table 3 Reactions at Room Temperature and Ambient Pressure[a]

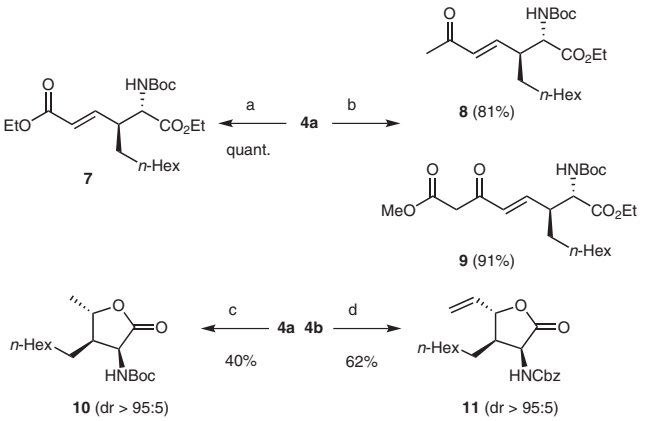


6 4, 5

Entry	Imine		Yield (%)[b]	dr[c]	ee (%)[d]
1[e]		**4a**	90	98:2	98
	6a				
2[e]		**4b**	86	99:1	93
	6b				
3		**5a**	73	89:11	84
	6c				
4		**5b**	76	93:7	78
	6d				

[a] Reaction conditions (0.24 mmol scale): olefin (4 equiv), Rh-catalyst (2.5 mol%; ratio [Rh]/L, 1:5).
[b] Yield determined by ^{1}H NMR spectroscopic analysis with 1,3,5-trimethoxybenzene as internal standard.
[c] Determined by ^{1}H NMR spectroscopic analysis of the crude mixture.
[d] Determined by chiral HPLC analysis, for details see the Supporting Information.
[e] Imine generated in situ from the corresponding α-amido sulfone with KF (5 equiv).

To explore the synthetic utility of the α-formyl amino acid derivatives **4**, the tandem product **4a** was subjected to a Horner–Wadsworth–Emmons reaction as well as to a Wittig olefination applying two stabilized ylides (Scheme 2). In all cases, excellent yields of the corresponding *E*-α,β-unsaturated carbonyl derivatives **7**–**9** were obtained. Interestingly, reaction of the tandem products **4a** and **4b** with Grignard reagents led to the stereoselective formation of the γ-lactones **10** and **11**, respectively, in excellent diastereoselectivity, albeit in moderate yield. A chelation model can explain the observed stereochemistry, which was assigned on the basis of the results of NOESY measurements.



Scheme 2 Follow-up chemistry of β-formyl-α-amino esters **4**. *Reagents and conditions*: (a) $(EtO)_2POCH_2CO_2Et$, NaH, CH_2Cl_2, 0 °C to r.t. 16 h; (b) $Ph_3PCHCOR$ (R = Me for **8**, R = CH_2CO_2Me for **9**), THF, r.t. 16 h; (c) MeMgBr (1 M in THF), Et_2O, –78 °C, 1 h, then –78 °C to r.t. 1 h; (d) $CH_2CHMgCl$ (1 M in THF), Et_2O, –78 °C, 1 h, then –78 °C to r.t. 1 h.

In conclusion, we have reported the first enantioselective tandem hydroformylation–organocatalytic *anti*-Mannich reaction. Starting from abundant α-olefins, C1-chain elongated functionalized and enolizable aldehydes were generated in situ through a highly regioselective hydroformylation. Simultaneously, reactive *N*-carbamoyl imines are generated through base-mediated elimination of tolyl sulfinic acid from stable α-amidosulfones. Enamine activation of the enolizable aldehyde by way of the chiral amine organocatalyst followed by addition to the imine (generated in situ) furnished the tandem hydroformylation–Mannich products **4** and **5** in good yields and high stereoselectivities. These α-formyl *N*-carbamoyl protected α-amino acid derivatives are highly versatile chiral building blocks, which allow for facile transformation into artificial and functionalized α-amino acid derivatives that are suitably functionalized for peptide chemistry.

All reactions were carried out in oven-dried glassware under an atmosphere of argon (Argon 5.0 from Sauerstoffwerke Friedrichshafen). All solvents were dried and distilled by standard procedures. Chromatographic purification of products was accomplished using flash chromatography[14] on Macherey–Nagel silica gel 60 (230–400 mesh).

Melting points were measured with a Büchi melting point apparatus using open glass capillaries, and the values are uncorrected. Elementary analyses were preformed with an Elementar vario (Elementar Analysensysteme GmbH). Optical rotations were measured with a Perkin–Elmer 241 polarimeter in 1.0 dm, 1.0 mL cells; the concentration (g/100 mL) and the solvent are given in parentheses. Chiral HPLC analyses were performed with Merck–Hitachi sys-

tems with Daicel Chiralpak AD-H (25 cm × 4.6 mm ID), Chiralpak AD-3 (15 cm × 4.6 mm ID), Chiralcel OD-H (25 cm × 4.6 mm ID), Chiralcel OJ-H (25 cm × 4.6 mm ID), Chiralcel OD-3 (15 cm × 4.6 mm ID), Chiralcel OJ-R (15 cm × 4.6 mm ID) or Chiralpak IA (25 cm × 4.6 mm ID) columns in *n*-heptane–isopropanol or *n*-heptane–ethanol mixtures.

NMR spectra were acquired with a Bruker AMX 400 spectrometer (400.132 and 100.626 MHz for ^{1}H and ^{13}C, respectively) and referenced internally according to residual proton solvent signals [$CDCl_3$: δ = 7.26 ppm (^{1}H); δ = 77.10 ppm (^{13}C)].[15] Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ, ppm), multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; m_c, symmetrical multiplet), coupling constant (Hz), assignment, integration. Data for ^{13}C NMR are reported in terms of chemical shift, assignment, integration. Low-resolution mass spectra were recorded with Thermo TSQ 700 spectrometers [EI: 70 eV; CI (NH_3): 110 eV]. High-resolution mass spectra were obtained with a Finnigan MAT 95XL instrument [EI: 70 eV; CI (NH_3): 110 eV].

The following substrates were purchased from commercial sources: 1-octene (Acros, distilled prior to use), 4-vinyl-1-cyclohexene (Acros), 5-hexen-1-ol (Merck), 5-hexen-2-one (AlfaAesar), 3,3-dimethyl-1-butene (AlfaAesar), 1,7-octadiene (Acros), ethyl glyoxylate (Aldrich), benzyl carbamate (AlfaAesar), and K_2HPO_4 (Riedel-de-Haën). The following substrates were prepared according to literature procedures: 6-diphenylphosphanylpyridin-2(1*H*)-one (6-DPPon),[11a] *tert*-butyldimethylundec-10-enyloxysilane,[16] hex-5-enyl acetate,[17] hex-5-enyloxymethylbenzene,[18] 2-dec-9-enyl[1,3]dioxolane,[19] undec-10-enoic acid methylphenylamide,[20] hex-5-enyl benzoate,[21] *tert*-butyl carbamate.[22]

Ethyl *tert*-Butoxycarbonylamino(toluene-4-sulfonyl)acetate (2a)[23]

tert-Butyl carbamate (2.01 g, 17.2 mmol, 1.0 equiv), ethyl glyoxylate (50% in toluene, 21.4 mL, 22.1 g, 34.3 mmol, 2.0 equiv) and sodium *p*-toluenesulfinate (12.9 g, 51.5 mmol, 3.0 equiv) were dissolved in formic acid (50% in H_2O, 17.0 mL) and stirred for 1.5 d at r.t. The reaction mixture was then poured into ice water (20 mL) and the white crystals that were obtained were washed with water and dried in vacuo to give **2a**.

Yield: 3.46 g (9.78 mmol, 57%); mp 110 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (s, 9 H, *t*-Bu), 1.31 (t, $^3J_{Me–CH2}$ = 7.2 Hz, 3 H, CH_3), 2.44 (s, 3 H, CH_3-Tol), 4.33 (q, $^3J_{CH2–CH3}$ = 6.2 Hz, 2 H, CH_2), 5.56 (d, $^3J_{CH–NH}$ = 10.0 Hz, 1 H, CH), 5.77 (d, $^3J_{NH–CH}$ = 10.0 Hz, 1 H, NH), 7.35 (d, ^3J = 8.1 Hz, 2 H, *p*-Ar-H), 7.78 (d, ^3J = 8.2 Hz, 2 H, *p*-Ar-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3-ester, 1C), 21.8 (CH_3-Tol, 1C), 28.1 (CH_3, *t*-Bu, 3C), 63.5 (CH_2-ester, 1C), 73.5 (*t*-Bu, 1C), 81.5 (CH_2, 1C), 129.7 (Ar, 2C), 129.8 (Ar, 2C), 133.8 (Ar, 1C), 145.7 (Ar, 1C), 153.4 [C(O), 1C], 163.4 [C(O), 1C].

MS (CI, NH_3): *m*/*z* = 139.0 (15), 278.0 (29), 296.1 (100), 375.1 (1) [$M^+ + NH_4^+$].

The analytical data correspond to those reported previously.[23]

Ethyl Benzyloxycarbonylamino(toluene-4-sulfonyl)acetate (2b)[23]

Benzylcarbamate (117 mg, 1.00 mmol, 1.0 equiv), ethyl glyoxylate (50% in toluene, 1.3 mL, 1.3 g, 2.0 mmol, 2.0 equiv) and sodium *p*-toluenesulfinate (535 mg, 3.00 mmol, 3.0 equiv) were dissolved in formic acid (1.0 mL) and stirred for 2 d at r.t. The reaction mixture was then poured into ice water (2 mL) and the white crystals were washed with water and dried in vacuo to give **2b**.

Yield: 276 mg (0.70 mmol, 70%); mp 95 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31 (t, $^3J_{Me–CH2}$ = 7.2 Hz, 3 H, CH_3), 2.45 (s, 3 H, CH_3-Tol), 4.31 (q, $^3J_{CH2–CH3}$ = 6.2 Hz, 2 H, CH_2), 5.03 (s, 2 H, CH_2-Bn), 5.62 (d, $^3J_{CH–NH}$ = 10.0 Hz, 1 H, CH), 6.05 (d, $^3J_{NH–CH}$ = 10.8 Hz, 1 H, NH), 7.20–7.42 (m, 7 H, Ar-H), 7.78 (d, ^3J = 7.3 Hz, 2 H, *o*-Ar-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0 (CH_3-ester, 1C), 21.9 (CH_3-Tol, 1C), 63.6 (CH_2-ester, 1C), 67.9 (CH_2-Bn, 1C), 73.9 (CH, 1C), 128.1 (Ar, 1C), 128.2 (Ar, 1C), 128.3 (Ar, 1C), 128.5 (Ar, 1C), 128.7 (Ar, 1C), 129.6 (Ar, 1C), 129.8 (Ar, 1C), 129.9 (Ar, 1C), 130.0 (Ar, 1C), 133.6 (Ar, 1C), 135.5 (Ar, 1C), 145.9 (Ar, 1C), 154.8 [C(O), 1C], 163.3 [C(O), 1C].

MS (CI, NH_3): *m*/*z* = 91.0 (93), 108.0 (36), 139.0 (48), 192.1 (85), 251.1 (45), 392.1 (18) [$M^+ + H$], 409.1 (100) [$M^+ + NH_4^+$].

The analytical data correspond to those reported previously.[23]

Domino Hydroformylation–*anti*-Mannich Reaction; General Procedure

A steel autoclave, equipped with a gas inlet, was charged with K_2HPO_4 (188 mg, 1.08 mmol, 3.0 equiv) and dried for 15 min under high vacuum. Under an inert atmosphere, $CHCl_3$ (0.24 M, 1.35 mL) and a solution of [$Rh(CO)_2$acac] (50 or 100 μL of a stock solution containing 1.8 mg in 400 μL $CHCl_3$) and 6-DPPon (100 or 200 μL of a stock solution containing 5.0 mg in 400 μL $CHCl_3$) were added successively, followed by addition of the olefin (0.54 mmol, 1.5 equiv), organocatalyst **1** (43 mg, 80 μmol, 0.20 equiv), 1,3,5-trimethoxybenzene (9.1 mg, 54 μmol, 0.15 equiv) and α-amido sulfone **2** (0.36 mmol, 1.0 equiv). The reaction mixture was saturated with synthesis gas (CO/H_2, 1:1) by applying three cycles of careful evacuating and refilling. The autoclave was pressurized with 20 bar CO/H_2 (1:1) and the mixture was stirred for 24 h at 45 °C. After cooling to r.t. and depressurization, the turbid mixture was diluted with CH_2Cl_2, filtered through a plug of silica, and washed with CH_2Cl_2–Et_2O (1:1). The solvent was removed in vacuo and the residue was purified by flash column chromatography (cyclohexane–EtOAc) to give amino carbonyl compound **4a–l**. The enantiomeric excess was determined by chiral HPLC analysis (UV detector); compounds that were not UV active were converted into the corresponding *O*-benzyloxime and then reduced (see the Supporting Information).

Ethyl (2*S*,3*R*)-2-(*tert*-Butoxycarbonylamino)-3-formyldecanoate (4a)

Prepared according to the general procedure with 1-octene (84 μL, 61 mg, 0.54 mmol, 1.5 equiv) and α-amido sulfone **2a** (129 mg, 0.360 mmol, 1.0 equiv). Purification was achieved by flash column chromatography (cyclohexane–EtOAc, 10:1).

Yield: 120 mg (0.350 mmol, 97%); colorless oil; $[\alpha]_D^{22}$ +25.4 (*c* = 1.50, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, $^3J_{Me–CH2}$ = 7.1 Hz, 3 H, CH_3), 1.25–1.35 (m, 10 H, CH_2), 1.37–1.46 (m, 11 H, CH_2, *t*-Bu), 3.05 (m_c, 0.8 H, CH), 2.72* (m_c, 0.2 H, CH), 4.18 (q, $^3J_{CH2–CH3}$ = 7.1 Hz, 2 H, CH_2), 4.56 (dd, $^3J_{CH–CH}$ = 4.0 Hz, $^3J_{CH–NH}$ = 9.5 Hz, 0.8 H, CH), 4.68* (dd, $^3J_{CH–CH}$ = 4.2 Hz, $^3J_{CH–NH}$ = 8.4 Hz, 0.2 H, CH), 5.24 (d, $^3J_{NH–CH}$ = 9.3 Hz, 1 H, NH), 9.60 (s, 1 H, CH), 9.68* (d, $^3J_{CH–CH}$ = 1.6 Hz, 1 H, CH). * = diastereomer.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3, 1C), 14.2 (CH_3, 1C), 25.2 (CH_2, 1C), 27.4 (CH_2, 1C), 28.3 (CH_2, 1C), 28.4 (CH_3, *t*-Bu, 3C), 20.0 (CH_2, 1C), 29.5 (CH_2, 1C), 31.8 (CH, 1C), 52.3 (CH, 1C), 53.1 (CH, 1C), 54.0 (CH, 1C), 61.8 (CH_2-ester, 1C), 171.3 (C, 1C), 201.4 (C(O), 1C), 202.6 (C(O), 1C).

Anal. Calcd for $C_{18}H_{33}NO_5$: C, 62.95; H, 9.68; N, 4.08. Found: C, 63.04; H, 9.71; N, 3.81.

Ethyl (2*S*,3*R*)-2-(Benzyloxycarbonylamino)-3-formyldecanoate (4b)

Prepared according to the general procedure with 1-octene (84 μL, 61 mg, 0.54 mmol, 1.5 equiv) and α-amido sulfone **2b** (141 mg, 0.360 mmol, 1.0 equiv). Purification was achieved by flash column chromatography (cyclohexane–EtOAc, 10:1).

Yield: 133 mg (0.350 mmol, 98%); colorless oil; 99% ee determined by chiral HPLC [Chiralpak-AD-H; 25 cm × 4.6 mm ID; *n*-heptane–*i*-PrOH, 90:10; 1.0 mL/min; λ = 214, 254 nm]: t_R = 10.8 (major), 11.6 (minor) min; $[\alpha]_D^{22}$ +35.6 (*c* = 0.48, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, $^3J_{Me–CH2}$ = 7.2 Hz, 3 H, CH_3), 1.25 (m_c, 10 H, CH_2), 1.42–1.50 (m, 2 H, CH_2), 3.11 (m_c, 1 H, CH), 2.75* (m_c, 1 H, CH), 4.19 (q, $^3J_{CH2–CH3}$ = 7.2 Hz, 2 H, CH_2), 4.63 (dd, $^3J_{CH–CH}$ = 3.7 Hz, $^3J_{CH–NH}$ = 9.5 Hz, 1 H, CH), 4.74* (dd, $^3J_{CH–CH}$ = 3.9 Hz, $^3J_{CH–NH}$ = 8.4 Hz, 1 H, CH), 5.14 (s, 2 H, CH_2), 5.52 (d, $^3J_{NH–CH}$ = 9.6 Hz, 1 H, NH), 7.14 (m_c, 5 H, Ar-H), 9.60 (s, 1 H, CH), 9.69* (s, 1 H, CH). * = diastereomer.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3, 1C), 14.2 (CH_3, 1C), 25.2 (CH_2, 1C), 27.5 (CH_2, 1C), 29.0 (CH_2, 1C), 29.5 (CH_2, 1C), 31.8 (CH_2, 1C), 49.3 (CH, 1C), 52.7 (CH, 1C), 53.8 (CH, 1C), 54.1 (CH, 1C), 62.1 (CH_2-ester, 1C), 67.3 (CH_2, 1C), 128.1 (Ph-C, 1C), 128.2 (Ph-C, 2C), 128.6 (Ph-C, 2C), 136.2 (Ph-C, 1C), 200.8 [C(O), 1C], 201.5 [C(O), 1C].

Anal. Calcd for $C_{21}H_{31}NO_5$: C, 66.82; H, 8.28; N, 3.71. Found: C, 66.86; H, 8.12; N, 3.57.

Ethyl (2*S*,3*R*)-2-(*tert*-Butoxycarbonylamino)-3-formyl-5,5-dimethyl-hexanoate (4c)

Prepared according to the general procedure with 3,3-dimethylbut-1-ene (77 μL, 45 mg, 0.54 mmol, 1.5 equiv) and α-amido sulfone **2a** (129 mg, 0.360 mmol, 1.0 equiv). Purification was achieved by flash column chromatography (cyclohexane–EtOAc, 10:1).

Yield: 79 mg (0.25 mmol, 70%); colorless oil; $[\alpha]_D^{22}$ +6.7 (*c* = 1.2, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (s, 9 H, *t*-Bu), 1.25 (t, $^3J_{Me–CH2}$ = 7.1 Hz, 3 H, CH_3), 1.32 (dd, $^3J_{CHA–CH}$ = 7.1 Hz, $^3J_{CHA–CHB}$ = 15.1 Hz, 1 H, CH_A), 1.46 (s, 9 H, *t*-Bu), 1.70 (dd, $^3J_{CHB–CH}$ = 6.8 Hz, $^3J_{CHB–CHA}$ = 14.5 Hz, 1 H, CH_B), 3.08 (m_c, 0.8 H, CH), 2.80* (m_c, 0.2 H, CH), 4.18 (q, $^3J_{CH2–CH3}$ = 7.1 Hz, 2 H, CH_2), 4.60 (dd, $^3J_{CH–CH}$ = 4.0 Hz, $^3J_{CH–NH}$ = 8.3 Hz, 0.8 H, CH), 4.50* (m_c, 0.2 H, CH), 5.33 (d, $^3J_{NH–CH}$ = 8.3 Hz, 1 H, NH), 9.62 (s, 0.9 H, CH), 9.70* (d, $^3J_{CH–CH}$ = 1.6 Hz, 1 H, CH). * = diastereomer.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3, 1C), 21.8 (CH, 1C), 28.4 (CH_3, *t*-Bu, 3C), 29.3 (CH_3, *t*-Bu, 3C), 37.2 (CH_2, 1C), 50.3 (CH, 1C), 54.2 (CH, 1C), 62.0 (CH_2-ester, 1C), 129.7 [C(O), 1C], 129.8 [C(O), 1C], 202.0 [C(O), 1C].

MS (APCI, +ve): *m*/*z* = 216.0 (36), 259.8 (51), 276.8 (39), 315.6 (100) $[M]^+$, 316.6 (21), 332.6 (44), 374.7 (63).

Ethyl (2*S*,3*R*)-2-Benzyloxycarbonylamino-3-formyl-4-(cyclohex-3-enyl)butyrate (4d)

Prepared according to the general procedure with 4-vinylcyclohex-1-ene (58 mg, 0.54 mmol, 1.5 equiv) and α-amido sulfone **2b** (141 mg, 0.360 mmol, 1.0 equiv). Purification was achieved by flash column chromatography (cyclohexane–EtOAc, 10:1).

Yield: 88 mg (0.32 mmol, 88%); colorless oil; 94% ee determined by chiral HPLC (Chiralpak-OJ-H; 25 cm × 4.6 mm ID; *n*-heptane–EtOH, 200:1; 1.0 mL/min; 40 °C; λ = 210 nm): t_R = 65.2 (major), 76.3 (major), 85.1 (minor), 90.8 (minor) min; $[\alpha]_D^{22}$ +37.5 (*c* = 1.00, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.23 (t, $^3J_{Me–CH2}$ = 7.1 Hz, 3 H, CH_3), 1.41–1.52 (m, 2 H, CH_2, CH), 1.70 (m_c, 4 H, CH, CH_2), 2.10 (m_c, 1 H, CH_2), 3.27 (m_c, 0.8 H, CH), 2.95* (m_c, 0.2 H, CH), 4.19 (q, $^3J_{CH2–CH3}$ = 6.0 Hz, 2 H, CH_2), 4.62 (dd, $^3J_{CH–CH}$ = 3.2 Hz, $^3J_{CH–NH}$ = 9.0 Hz, 0.8 H, CH), 4.71* (dd, $^3J_{CH–CH}$ = 3.4 Hz, $^3J_{CH–NH}$ = 8.2 Hz, 0.2 H, CH), 5.12 (s, 2 H, CH_2), 5.55 (d, $^3J_{NH–CH}$ = 10.1 Hz, 1 H, NH), 5.65 (m_c, 2 H, CH), 7.31–7.46 (m, 5 H, Ar-H), 9.60 (s, 0.4 H, $CH_{Aldehyde}$), 9.62 (s, 0.4 H, $CH_{Aldehyde}$), 9.71* (s, 0.1 H, $CH_{Aldehyde}$), 9.73* (s, 0.1 H, $CH_{Aldehyde}$). * = diastereomer.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3, 1C), 24.9 (CH_2, 1C), 28.3 (CH_2, 1C), 29.0 (CH_2, 1C), 30.9 (CH_2, 1C), 31.0 (CH, 1C), 51.2 (CH, 1C), 52.0 (CH, 1C), 62.1 (CH_2-ester, 1C), 67.2 (CH_2, 1C), 127.0 (CH, 2C), 127.3 (Ar-C, 1C), 128.1 (Ar-C, 2C), 128.3 (Ar-C, 2C), 128.6 (Ar-C, 1C), 156.5 [C(O), 1C], 170.8 [C(O), 1C], 202.4 [C(O), 1C].

MS (CI, NH_3): *m*/*z* = 91.0 (25), 360.2 (24), 374.2 (100) $[M^+ + H]$.

HRMS (CI): *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{28}NO_5$: 374.19670; found: 374.19675 (Δ: 0.1 ppm).

Ethyl (2*S*,3*R*)-2-*tert*-Butoxycarbonylamino-3-formyl-8-hydroxyoctanoate (4e)

Prepared according to the general procedure with hex-5-en-1-ol (84 μL, 61 mg, 0.54 mmol, 1.5 equiv) and α-amido sulfone **2a** (129 mg, 0.360 mmol, 1.0 equiv). Purification was achieved by flash column chromatography (cyclohexane–EtOAc, 5:1).

Yield: 99 mg (0.30 mmol, 83%); colorless oil; $[\alpha]_D^{22}$ +26.5 (*c* = 1.30, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.22 (t, $^3J_{Me–CH2}$ = 7.2 Hz, 3 H, CH_3), 1.42 (s, 3 H, *t*-Bu), 1.55 (m_c, 4 H, CH_2), 1.65–1.84 (m, 4 H, CH_2), 3.05 (m_c, 0.8 H, CH), 2.75* (m_c, 0.2 H, CH), 3.60–3.66 (m, 2 H, CH_2), 4.17 (q, $^3J_{CH2–CH3}$ = 7.2 Hz, 2 H, CH_2), 4.56 (dd, $^3J_{CH–CH}$ = 3.7 Hz, $^3J_{CH–NH}$ = 9.4 Hz, 0.8 H, CH), 4.67* (m_c, 0.2 H, CH), 5.27 (d, $^3J_{NH–CH}$ = 9.2 Hz, 1 H, NH), 9.58 (s, 0.8 H, $CH_{Aldehyde}$), 9.64* (d, $^3J_{CH–CH}$ = 1.5 Hz, 0.2 H, $CH_{Aldehyde}$). * = diastereomer.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3, 1C), 25.0 (CH_2, 1C), 25.7 (CH_2, 1C), 28.3 (CH_3, *t*-Bu, 3C), 30.3 (CH_2, 1C), 32.2 (CH_2, 1C), 46.3 (CH, 1C), 52.1 (CH, 1C), 53.9 (CH, 1C), 61.9 (CH_2, 1C), 62.6 (CH_2-ester, 1C), 171.3 (C, 1C), 202.4 [C(O), 1C], 205.2 [C(O), 1C].

MS (APCI, +ve): *m*/*z* = 232.1 (96), 257.8 (82), 331.8 (100) $[M]^+$, 348.8 (72), 654.0 (60).

Anal. Calcd for $C_{16}H_{29}NO_6$: C, 57.99; H, 8.82; N, 4.23. Found: C, 57.90; H, 8.87; N, 4.06.

Ethyl (2*S*,3*R*)-8-Benzyloxy-2-*tert*-butoxycarbonylamino-3-formyl-octanoate (4f)

Prepared according to the general procedure with 1-[(hex-5-enyloxy)methyl]benzene (103 mg, 0.540 mmol, 1.5 equiv) and α-amido sulfone **2a** (129 mg, 0.360 mmol, 1.0 equiv). Purification was achieved by flash column chromatography (cyclohexane–EtOAc, 10:1).

Yield: 129 mg (0.310 mmol, 85%); colorless oil; 94% ee determined by chiral HPLC (Chiralpak-AD-H; 25 cm × 4.6 mm ID; *n*-heptane–*i*-PrOH, 95:5; 1.0 mL/min; λ = 214 nm): t_R = 15.6 (major), 17.2 (minor) min; $[\alpha]_D^{22}$ +23.6 (*c* = 0.48, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.18 (t, $^3J_{Me–CH2}$ = 7.2 Hz, 3 H, CH_3), 1.25–1.45 (m, 4 H, CH_2), 1.37 (s, 9 H, *t*-Bu), 1.55 (m_c, 2 H, CH_2), 1.62–1.78 (m, 2 H, CH_2), 2.98 (m_c, 0.7 H, CH), 2.66* (m_c, 0.3 H, CH), 3.40 (t, $^3J_{CH2–CH2}$ = 6.6 Hz, 2 H, CH_2), 4.12 (q, $^3J_{CH2–CH3}$ = 7.2 Hz, 2 H, CH_2), 4.42 (s, 0.5 H, CH_2), 4.43* (s, 1.5 H, CH_2), 4.45 (dd, $^3J_{CH–CH}$ = 3.8 Hz, $^3J_{CH–NH}$ = 9.5 Hz, 0.8 H, CH), 4.61* (m_c, 0.2 H, CH), 5.19 (d, $^3J_{NH–CH}$ = 9.2 Hz, 1 H, NH), 7.20–7.32 (m, 5 H, Ar-H), 9.53 (s, 0.8 H, CH), 9.61* (d, $^3J_{CH–CH}$ = 1.1 Hz, 0.2 H, CH). * = diastereomer.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3, 1C), 25.1 (CH_2, 1C), 28.0 (CH_2, 1C), 28.3 (CH_2, 1C), 28.4 (*t*-Bu, 3C), 29.5 (CH_2, 1C), 29.6 (CH_2, 1C), 52.3 (CH, 1C), 53.0 (CH, 1C), 53.9 (CH, 1C), 61.9 (CH_2-ester, 1C), 70.2 (CH_2, 1C), 73.0 (CH_2, 1C), 127.6 (Ph-C, 1C), 127.7 (Ph-C, 2C), 128.4 (Ph-C, 2C), 138.7 (Ph-C, 1C), 171.2 (*t*-Bu, 1C), 201.3 [C(O), 1C], 202.4 [C(O), 1C].

MS (APCI, +ve): *m*/*z* = 322.1 (52), 421.7 (100) $[M]^+$, 438.9 (64), 454.3 (30).

HRMS (CI): *m*/*z* $[M + H]^+$ calcd for $C_{23}H_{36}NO_6$: 422.25440; found: 422.25426 (Δ: –0.3 ppm).

Ethyl (2*S*,3*R*)-2-Benzyloxycarbonylamino-13-(*tert*-butyldimethylsilanyloxy)-3-formyl-tridecanoate (4g)

Prepared according to the general procedure with *tert*-butyldimethyl(undec-10-enyloxy)silane (154 mg, 0.540 mmol, 1.5 equiv) and α-amido sulfone **2b** (141 mg, 0.360 mmol, 1.0 equiv). Purification was achieved by flash column chromatography (cyclohexane–EtOAc, 20:1).

Yield: 182 mg (0.331 mmol, 92%); colorless oil; 93% ee determined by chiral HPLC (Chiralpak-AD-H; 25 cm × 4.6 mm ID; *n*-heptane–EtOH, 95:5; 1.0 mL/min; λ = 210 nm): t_R = 6.2 (major), 7.1 (minor) min; $[\alpha]_D^{22}$ +23.28 (*c* = 1.04, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.05 (s, 6 H, CH_3), 0.90 (s, 9 H, *t*-Bu), 1.25 (t, $^3J_{Me–CH2}$ = 7.2 Hz, 3 H, CH_3), 1.29 (m_c, 14 H, CH_2), 1.50 (m_c, 4 H, CH_2), 3.12 (m_c, 0.8 H, CH), 2.72* (m_c, 0.2 H, CH), 3.59 (t, $^3J_{CH2–CH2}$ = 6.6 Hz, 2 H, CH_2), 4.18 (q, $^3J_{CH2–CH3}$ = 7.2 Hz, 2 H, CH_2), 4.63 (dd, $^3J_{CH–CH}$ = 3.8 Hz, $^3J_{CH–NH}$ = 9.5 Hz, 0.8 H, CH), 4.74* (dd, $^3J_{CH–CH}$ = 3.8 Hz, $^3J_{CH–NH}$ = 8.4 Hz, 0.2 H, CH), 5.14 (s, 1.6 H, CH_2), 5.10* (s, 0.4 H, CH_2), 5.51 (d, $^3J_{NH–CH}$ = 9.6 Hz, 0.9 H, NH), 5.47* (d, $^3J_{NH–CH}$ = 8.4 Hz, 0.1 H, NH), 7.30–7.40 (m, 5 H, Ph), 9.61 (s, 0.9 H, $CH_{Aldehyde}$), 9.69* (d, $^3J_{CH–CH}$ = 1.5 Hz, 0.1 H, $CH_{Aldehyde}$). * = diastereomer.

^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.2 (CH_3, 2C), 14.1 (CH_3, 1C), 18.5 (CH_2, 1C), 25.1 (CH_2, 1C), 25.2 (CH_2, 2C), 25.9 (CH_2, 1C), 26.1 (CH_3, *t*-Bu, 3C), 27.5 (CH_2, 1C), 29.4 (CH_2, 2C), 29.5 (CH_2, 1C), 52.7 (CH, 1C), 53.8 (CH, 1C), 62.0 (CH_2-ester, 1C), 63.4 (CH_2, 1C), 67.2 (CH_2, 1C), 128.1 (Ar-C, 1C), 128.3 (Ar-C, 2C), 128.6 (Ar-C, 2C), 128.7 (Ar-C, 1C), 136.3 (*t*-Bu, 1C), 156.6* [C(O), 1C], 171.0* [C(O), 1C], 202.6* [C(O), 1C], 202.5 ($CH_{Aldehyde}$, 1C), [201.3* ($CH_{Aldehyde}$, 1C)]. * = diastereomer.

HRMS (CI): *m*/*z* $[M + H]^+$ calcd for $C_{30}H_{52}NO_6Si$: 550.35639; found: 550.35540 (Δ: 1.8 ppm).

Ethyl (2*S*,3*R*)-8-Acetoxy-2-*tert*-butoxycarbonylamino-3-formyloctanoate (4h)

Prepared according to the general procedure with hex-5-enyl acetate (77 mg, 0.54 mmol, 1.5 equiv) and α-amido sulfone **2a** (129 mg, 0.360 mmol, 1.0 equiv). Purification was achieved by flash column chromatography (cyclohexane–EtOAc, 10:1).

Yield: 132 mg (0.350 mmol, 98%); colorless oil; $[\alpha]_D^{22}$ +32.4 (*c* = 1.00, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25 (t, $^3J_{Me–CH2}$ = 7.2 Hz, 3 H, CH_3), 1.35–1.45 (m_c, 6 H, CH_2), 1.48 (s, 9 H, *t*-Bu), 1.52–1.62 (m, 2 H, CH_2), 2.05 (s, 3 H, CH_3), 3.05 (m_c, 0.9 H, CH), 2.54* (m_c, 0.1 H, CH), 4.10 (m_c, 2 H, CH_2), 4.18 (q, $^3J_{CH2–CH3}$ = 7.2 Hz, 2 H, CH_2), 4.58 (dd, $^3J_{CH–NH}$ = 3.7 Hz, $^3J_{CH–CH}$ = 8.8 Hz, 0.9 H, CH), 4.68* (m_c, 0.1 H, CH), 5.25 (d, $^3J_{NH–CH}$ = 9.4 Hz, 1 H, NH), 9.61 (s, 0.9 H, $CH_{Aldehyde}$), 9.69* (d, $^3J_{CH–CH}$ = 1.5 Hz, 0.1 H, $CH_{Aldehyde}$). * = diastereomer.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0 (CH_3, 1C), 14.1 (CH_3, 1C), 21.0 (CH_2, 1C), 23.5 (CH_2, 1C), 23.7 (CH_2, 1C), 28.40 (*t*-Bu, 3C), 29.1 (CH_2, 1C), 46.3 (CH, 1C), 63.5 (CH, 1C), 64.3 (CH_2-ester, 1C), 73.5 (CH_2, 1C), 145.9 [C(O), 1C], 181.0 [C(O), 1C], 205.0 [C(O), 1C].

MS (CI, NH_3): *m*/*z* = 200.1 (43), 274.2 (100), 318.2 (62), 335.2 (40), 374.2 (11) $[M^+ + H]$.

HRMS (CI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{32}NO_7$: 374.21788; found: 374.21730 (Δ: 1.5 ppm).

(2*S*,3*R*)-Ethyl 8-Benzoyloxy-2-*tert*-butoxycarbonylamino-3-formyl-octanoate (4i)

Prepared according to the general procedure with hex-5-enyl benzoate (103 mg, 0.500 mmol, 1.4 equiv) and α-amido sulfone **2a** (129 mg, 0.360 mmol, 1.0 equiv). Purification was achieved by flash column chromatography (cyclohexane–EtOAc, 10:1).

Yield: 119 mg (0.270 mmol, 76%); colorless oil; 93% ee determined by chiral HPLC (Chiralpak-AD-H; 25 cm × 4.6 mm ID; *n*-heptane–*i*-PrOH, 90:10; 1.0 mL/min; λ = 214 nm): t_R = 14.8 (major), 17.6 (minor) min; $[\alpha]_D^{22}$ +27.2 (*c* = 0.69, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (t, $^3J_{Me–CH2}$ = 7.2 Hz, 3 H, CH_3), 1.43 (s, 9 H, *t*-Bu), 1.51 (m_c, 4 H, CH_2), 1.78 (m_c, 4 H, CH_2), 3.07 (m_c, 0.7 H, CH), 2.75* (m_c, 0.3 H, CH), 4.20 (q, $^3J_{CH2–CH3}$ = 7.2 Hz, 2 H, CH_2), 4.32 (t, $^3J_{CH2–CH2}$ = 6.9 Hz, 2 H, CH_2), 4.58 (dd, $^3J_{CH–CH}$ = 3.8 Hz, $^3J_{CH–NH}$ = 9.3 Hz, 0.7 H, CH), 4.70* (dd, $^3J_{CH–CH}$ = 3.4 Hz, $^3J_{CH–NH}$ = 8.0 Hz, 0.3 H, CH), 5.25 (d, $^3J_{NH–CH}$ = 9.1 Hz, 1 H, NH), 7.44 (m_c, 2 H, Ar-H), 7.55 (m_c, 1 H, Ar-H), 8.04 (m_c, 2 H, Ar-H), 9.62 (s, 0.7 H, $CH_{Aldehyde}$), 9.69* (d, $^3J_{CH–CH}$ = 1.5 Hz, 0.3 H, $CH_{Aldehyde}$). * = diastereomer.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3, 1C), 27.2 (CH_2, 1C), 28.3 (CH_2, 1C), 28.4 (*t*-Bu, 3C), 28.5 (CH_2, 1C), 28.6 (CH_2, 1C), 52.2 (CH, 1C), 53.1 (CH, 1C), 54.0 (CH, 1C), 61.9 (CH_2-ester, 1C), 64.9 (CH_2, 1C), 128.4 (Ph-C, 2C), 129.6 (Ph-C, 2C), 132.9 (Ph-C, 1C), 166.7 (Ph-C, 1C), 201.1 [C(O), 1C], 202.2 [C(O), 1C].

MS (CI, NH_3): *m*/*z* = 336.0 (23), 435.6 (98) $[M]^+$, 452.5 (100), 757.9 (18).

Anal. Calcd for $C_{23}H_{33}NO_7$: C, 63.43; H, 7.64; N, 3.22. Found: C, 63.68; H, 7.70; N, 3.47.

Ethyl (2*S*,3*R*)-(2-*tert*-Butoxycarbonylamino)-3-formyl-12-(methylphenylcarbamoyl)dodecanoate (4j)

Prepared according to the general procedure with *N*-methyl-*N*-phenylundec-10-enamide (145 mg, 0.540 mmol, 1.5 equiv) and α-amido sulfone **2a** (129 mg, 0.360 mmol, 1.0 equiv). Purification was achieved by flash column chromatography (cyclohexane–EtOAc, 10:1).

Yield: 174 mg (0.345 mmol, 96%) colorless oil; 99% ee determined by chiral HPLC (Chiralpak-IA; 25 cm × 4.6 mm ID; *n*-heptane–1,4-dioxane, 85:15; 1.0 mL/min; λ = 214 nm): t_R = 18.6 (major), 9.4 (minor) min; $[\alpha]_D^{22}$ +22.6 (*c* = 0.83, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.10–1.21 (m_c, 8 H, CH_2), 1.25 (t, $^3J_{Me–CH2}$ = 7.1 Hz, 3 H, CH_3), 1.22–1.30 (m_c, 6 H, CH_2), 1.42 (s, 9 H, *t*-Bu), 1.55 (m_c, 2 H, CH_2), 2.05 (m_c, 2 H, CH_2), 3.02 (m_c, 10.8 H, CH), 2.71* (m_c, 0.2 H, CH), 3.25 (s, 3 H, CH_3), 4.18 (q, $^3J_{CH2–CH3}$ = 6.9 Hz, 2 H, CH_2), 4.54 (dd, $^3J_{CH–CH}$ = 3.5 Hz, $^3J_{CH–NH}$ = 9.5 Hz, 0.8 H, CH), 4.67* (m_c, 0.2 H, CH), 5.24 (d, $^3J_{NH–CH}$ = 9.5 Hz, 1 H, NH), 7.15 (m_c, 2 H, Ar-H), 7.34 (m_c, 1 H, Ar-H), 7.40 (m_c, 2 H, Ar-H), 9.59 (s, 0.8 H, $CH_{Aldehyde}$), 9.66* (d, $^3J_{CH–CH}$ = 1.5 Hz, 0.2 H, $CH_{Aldehyde}$). * = diastereomer.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3, 1C), 25.6 (CH_2, 1C), 27.4 (CH_2, 1C), 28.3 (CH_2, 1C), 28.4 (*t*-Bu, 3C), 29.3 (CH_2, 2C), 29.4 (CH_2, 1C), 29.5 (CH_2, 1C), 34.1 (CH_2, 1C), 37.4 (CH_3, 1C), 52.3 (CH, 1C), 53.1 (CH, 1C), 53.9 (CH, 1C), 61.8 (CH_2-ester, 1C), 127.4 (Ph-C, 1C), 127.7 (Ph-C, 2C), 129.8 (Ph-C, 2C), 144.4 (Ph-C, 1C), 171.3 [C(O), 1C], 201.4 [C(O)O, 1C], 202.6 [C(O)O, 1C].

MS (APCI, +ve): *m*/*z* = 388.1 (12), 405.0 (7), 448.8 (18), 504.8 (100) $[M]^+$, 505.9 (26) $[M^+ + H]$, 520.9 (15).

HRMS (CI): *m*/*z* $[M + H]^+$ calcd for $C_{28}H_{45}N_2O_6$: 505.32776; found: 505.32860 (Δ: –1.7 ppm).

Ethyl (2*S*,3*R*)-2-*tert*-Butoxycarbonylamino-12-[1,3]dioxolan-2-yl-3-formyldodecanoate (4k)

Prepared according to the general procedure with 2-(dec-9-enyl)-1,3-dioxolane (127 μL, 115 mg, 0.540 mmol, 1.5 equiv) and α-amido sulfone **2a** (129 mg, 0.36 mmol, 1.0 equiv). Purification was achieved by flash column chromatography (cyclohexane–EtOAc, 15:1).

Yield: 136 mg (0.306 mmol, 85%); $[\alpha]_D^{22}$ +7.2 (*c* = 1.10, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.20–1.35 (m, CH_2, 15 H, CH_3), 1.20–1.35 (m, 2 H, CH_2), 1.44 (s, 9 H, *t*-Bu), 1.56–1.64 (m, 2 H, CH_2), 1.68–1.80 (m, 2 H, CH_2), 3.04 (m_c, 0.8 H, CH), 2.71* (m_c, 0.2 H, CH), 3.82 (m_c, 2 H, CH_2), 3.95 (m_c, 2 H, CH_2), 4.18 (q, $^3J_{CH2–CH3}$ = 7.2 Hz, 2 H, CH_2), 4.55 (dd, $^3J_{CH–CH}$ = 3.8 Hz, $^3J_{CH–NH}$ =

9.4 Hz, 0.8 H, CH), 4.68* (dd, $^3J_{CH–CH}$ = 3.7 Hz, $^3J_{CH–NH}$ = 8.1 Hz, 0.2 H, CH), 4.82 (t, $^3J_{CH–CH2}$ = 4.8 Hz, 1 H, CH), 5.24 (d, $^3J_{NH–CH}$ = 9.6 Hz, 1 H), 9.58 (s, 0.8 H, $CH_{Aldehyde}$), 9.66* (d, $^3J_{CH–CH}$ = 1.5 Hz, 0.2 H, $CH_{Aldehyde}$). * = diastereomer.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3, 1C), 24.1 (CH_2, 1C), 25.1 (CH_2, 1C), 27.4 (CH_2, 2C), 28.3 (CH_2, 1C), 28.3 (CH_3, *t*-Bu, 3C), 29.3 (CH_2, 1C), 29.4 (CH_2, 2C), 29.5 (CH_2, 1C), 29.6 (CH_2, 1C), 52.3 (CH, 1C), 53.9 (CH, 1C), 54.6 (CH, 1C), 61.8 (CH_2-ester, 1C), 64.9 (CH_2, 2C), 171.3 (*t*-Bu, 1C), 201.4 [C(O), 1C], 202.5 [C(O), 1C].

MS (APCI, +ve): *m*/*z* = 344.1 (35), 387.9 (20), 443.7 (100) $[M]^+$, 459.3 (28).

HRMS (CI): *m*/*z* $[M + H]^+$ calcd for $C_{23}H_{42}NO_7$: 444.29613; found: 444.29610 (Δ: 0.1 ppm).

Diethyl (2S,11*S*,3R,10*R*)-2,11-Bis(*tert*-butoxycarbonylamino)-3,10-diformyl-dodecanedioate (4l)

Prepared according to the general procedure with octa-1,7-diene (26 mg, 0.23 mmol, 0.65 equiv) and α-amido sulfone **2a** (129 mg, 0.360 mmol, 1.0 equiv). Purification was achieved by flash column chromatography (cyclohexane–EtOAc, 10:1).

Yield: 173 mg (0.302 mmol, 84%); colorless oil; $[\alpha]_D^{22}$ +10.7 (*c* = 0.90, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25 (t, $^3J_{Me–CH2}$ = 7.2 Hz, 6 H, CH_3), 1.38–1.46 (m, 8 H, CH_2), 1.43 (s, 18 H, *t*-Bu), 1.62–1.85 (m, 4 H, CH_2), 3.04 (m_c, 1 H, CH), 2.73* (m_c, 1 H, CH), 4.20 (q, $^3J_{CH2–CH3}$ = 7.2 Hz, 4 H, CH_2), 4.55 (m, 1.3 H, CH), 4.67* (dd, $^3J_{CH–CH}$ = 3.7 Hz, $^3J_{CH–NH}$ = 7.8 Hz, 0.7 H, CH), 5.25 (d, $^3J_{NH–CH}$ = 9.6 Hz, 2 H, NH), 9.59 (s, 1.3 H, CH), 9.66* (s, 0.7 H, CH). * = diastereomer.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3, 2C), 23.6 (CH_2, 1C), 24.8 (CH_2, 1C), 25.1 (CH_2, 1C), 27.0 (CH_2, 1C), 27.4 (CH_2, 1C), 28.3 (CH_2, 1C), 28.4 (CH_3, *t*-Bu, 6C), 29.2 (CH, 1C), 61.9 (CH_2-ester, 2C), 155.3 (C, 1C), 155.9 (C, 1C), 170.9 [C(O), 1C], 171.2 [C(O), 1C], 201.3 [C(O), 1C], 202.4 [C(O), 1C].

MS (APCI, +ve): *m*/*z* = 417.0 (100), 516.7 (32), 572.7 (94) $[M]^+$, 589.7 (76), 741.8 (20).

Domino Reaction under RTAP Conditions; General Procedure

$[Rh(CO)_2acac]$ (2.5 mg, 9.7 μmol, 0.025 equiv) and 6-DPPon (13.5 mg, 48 μmol, 0.125 equiv) were dissolved in a Schlenk flask in $CHCl_3$ (1.5 mL) and stirred for 5 min at r.t. After the addition of 1-octene (230 μL, 163 mg, 1.45 mmol, 4.0 equiv) the mixture was stirred for 3 min, then aminocatalyst **1** (43 mg, 80 μmol, 0.20 equiv) and trimethoxybenzene (9.1 mg, 54 μmol, 0.15 equiv) were successively added. After addition of either the corresponding α-amidosulfone **2** (0.36 mmol, 1.0 equiv) and KF (105 mg, 1.80 mmol, 5.0 equiv) or the corresponding imine **6a**–**d** (0.36 mmol, 1.0 equiv), the reaction mixture was saturated with synthesis gas (CO/H_2, 1:1) by applying three cycles of careful evacuation and refilling. The flask was pressurized with 1 bar CO/H_2 (1:1) and the mixture was stirred for 24 h at r.t. After depressurization, the mixture was diluted with CH_2Cl_2, filtered through a plug of silica where appropriate and washed with CH_2Cl_2–Et_2O (1:1). The solvent was removed in vacuo and the residue was purified by flash column chromatography (cyclohexane–EtOAc) giving the amino carbonyl compound **4** or **5**. The enantiomeric excess was determined by chiral HPLC analysis.

Ethyl (4-Methoxyphenylimino)acetate (6c)

To a solution of ethyl glyoxylate (50% in toluene, 2.5 mL, 2.6 g, 4.0 mmol, 1.0 equiv) in CH_2Cl_2 (15 mL), a solution of *p*-anisidine (0.50 g, 4.0 mmol, 1.0 equiv) in CH_2Cl_2 (5 mL) was added at r.t. The mixture was stirred for 30 min, then molecular sieves (4 Å) were added. After 1 h at r.t., the reaction mixture was filtered and concentrated in vacuo. Purification by flash column chromatography (cyclohexane–EtOAc, 5:1; silicagel deactivated with 5% Et_3N) gave **6c**. The analytical data correspond to those reported previously.[24]

Yield: 716 mg (3.50 mmol, 86%); yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.40 (t, $^3J_{Me–CH2}$ = 7.2 Hz, 3 H, CH_3), 3.81 (s, 3 H, OCH_3), 4.40 (q, $^3J_{CH2–CH3}$ = 7.1 Hz, 2 H, CH_2), 6.86 (d, ^3J = 9.0 Hz, 2 H, *o*-Ar-H), 7.35 (d, ^3J = 9.1 Hz, 2 H, *o*-Ar-H), 7.87 (s, 1 H, CH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.3 (s, CH_3, 1C), 55.6 (s, OCH_3, 1C), 62.0 (s, CH_2, 1C), 114.6 (s, Ar-CH, 2C), 123.7 (s, Ar-CH, 2C), 141.5 (s, Ar-C, 1C), 148.1 [s, C(N), 1C], 160.6 (s, Ar-C, 1C), 163.7 [s, C(O), 1C].

MS (EI): *m*/*z* = 77.0 (8), 107.0 (12), 134.0 (100), 207.1 (50) $[M]^+$.

***N*-Isobutylidene-4-methylbenzenesulfonamide (6d)**

A mixture of isobutyraldehyde (0.91 mL, 0.72 mg, 10 mmol, 1.0 equiv), toluenesulfonamide (1.7 g, 10 mmol, 1.0 equiv) and sodium *p*-toluenesulfinate (1.8 g, 10 mmol, 1.0 equiv) in formic acid (15 mL) and distilled H_2O (15 mL) was stirred for 12 h at r.t. The white precipitate was removed by filtration, washed with H_2O (2 × 10 mL) and cyclohexane (10 mL), then dissolved in CH_2Cl_2 (100 mL). Aqueous $NaHCO_3$ (70 mL) was added and the mixture was stirred for 2 h at r.t. After separation of the layers, the aqueous phase was extracted with CH_2Cl_2 (70 mL) and the combined organic phases were dried ($NaHCO_3$) to give **6d**. The analytical data correspond to those reported previously.[25]

Yield: 571 mg (2.50 mmol, 25%); colorless solid; mp 50 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.76 (d, $^3J_{CH–CH3}$ = 6.9 Hz, 6 H, CH_3), 1.93 (s, 3 H, CH_3), 2.10 (dsept, $^3J_{CH–CH}$ = 3.8 Hz, $^3J_{CH–CH3}$ = 1.1 Hz, 1 H, CH), 6.85 (d, ^3J = 8.0 Hz, 2 H, *o*-Ar-H), 8.03 (d, ^3J = 8.2 Hz, 2 H, *o*-Ar-H), 8.59 (d, $^3J_{CH–CH}$ = 3.9 Hz, 1 H, CH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.5 (s, CH_3, 2C), 21.1 (s, CH_3, 1C), 34.4 (s, CH, 1C), 128.4 (s, Ar-CH, 2C), 129.8 (s, Ar-CH, 2C), 136.4 (s, Ar-C, 1C), 144.1 (s, Ar-C, 1C), 181.2 [s, C(N), 1C].

MS (CI, NH_3): *m*/*z* = 155.1 (8), 226.2 (100) $[M]^+$, 243.1 (41) $[M^+ + NH_4]^+$.

Preparation and Characterization of 4a,b and 5a,b under RTAP Conditions

Ethyl (2*S*,3*R*)-2-*tert*-Butoxycarbonylamino-3-formyldecanoate (4a)

Prepared according to the general procedure with 1-octene (230 μL, 163 mg, 1.45 mmol, 4.0 equiv) and **6a** (129 mg, 0.360 mmol, 1.0 equiv). Purification was achieved by flash column chromatography (cyclohexane–EtOAc, 10:1) to obtain **4a**.

Yield: 111 mg (0.324 mmol, 90%); colorless oil; 98% ee determined by chiral HPLC of the corresponding *O*-benzyloxime (Chiralpak-AD-H; 25 cm × 4.6 mm ID; *n*-heptane–*i*-PrOH, 85:15; 1.0 mL/min; λ = 214 nm): t_R = 14.5 (major), 10.4 (minor) min; $[\alpha]_D^{22}$ +23.1 (*c* = 1.10, $CHCl_3$).

For analytical data, see above.

Ethyl (2*S*,3*R*)-2-Benzyloxycarbonylamino-3-formyldecanoate (4b)

Prepared according to the general procedure with 1-octene (230 μL, 163 mg, 1.45 mmol, 4.0 equiv) and **6b** (141 mg, 0.360 mmol, 1.0 equiv). Purification by flash column chromatography (cyclohexane–EtOAc, 10:1) gave **4b**.

Yield: 118 mg (0.310 mmol, 86%); colorless oil; 93% ee determined by chiral HPLC (Chiralpak-AD-H; 25 cm × 4.6 mm ID; *n*-heptane–*i*-PrOH, 85:15; 1.0 mL/min; λ = 214 nm): t_R = 10.8 (major), 11.5 (minor) min; $[\alpha]_D^{22}$ +39.1 (*c* = 1.20, $CHCl_3$).

For analytical data, see above.

Ethyl (2*S*,3*R*)-3-Formyl-2-(4-methoxyphenylamino)decanoate (5a)

Prepared according to the general procedure with 1-octene (230 µL, 163 mg, 1.45 mmol, 4.0 equiv) and ethyl (4-methoxyphenylimino)acetate (**6c**; 74 mg, 0.36 mmol, 1.0 equiv). Purification was achieved by flash column chromatography [cyclohexane–EtOAc, 50:1 → 10:1; Alox (deactivated with 8% H_2O)] to give **5a**.

Yield: 92 mg (0.263 mmol, 73%); yellow oil; 84% ee determined by chiral HPLC (Chiralpak-AD-3; 15 cm × 4.6 mm ID; *n*-heptane–*i*-PrOH, 98:2; 1.0 mL/min; λ = 214 nm): t_R = 4.3 (major), 4.8 (minor) min; $[\alpha]_D^{22}$ –19.3 (*c* = 1.00, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.83 (t, $^3J_{Me–CH2}$ = 7.1 Hz, 3 H, CH_3), 1.26 (m_c, 13 H, CH_2, CH_3), 1.55 (m_c, 2 H, CH_2), 2.76 (m_c, 1 H, CH), 2.95* (m_c, 1 H, CH), 3.81 (s, 3 H, OMe), 4.13 (q, $^3J_{CH2–CH3}$ = 7.1 Hz, 2 H, CH_2), 4.91 (d, $^3J_{CH–NH}$ = 10.2 Hz, 1 H, CH), 4.99 (d, $^3J_{NH–CH}$ = 17.5 Hz, 1 H, NH), 6.65 (d, ^3J = 9.4 Hz, 2 H, *o*-Ar-H), 6.79 (d, ^3J = 9.0 Hz, 2 H, *o*-Ar-H), 9.66 (d, $^3J_{CH–CH}$ = 2.7 Hz, 1 H, CH), 9.70* (d, $^3J_{CH–CH}$ = 2.3 Hz, 1 H, CH). * = diastereomer.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3, 3C), 22.7 (CH_2, 1C), 22.8 (CH_2, 1C), 25.5 (CH_3, 1C), 26.8 (CH_2, 1C), 28.9 (CH_2, 1C), 29.0 (CH_2, 1C), 29.5 (CH, 1C), 29.6 (CH_2, 1C), 30.0 (CH_2, 1C), 31.0 (CH_2, 1C), 53.7 (CH, 1C), 55.6 (OMe, 1C), 60.4 (CH_2, 1C), 114.3 (Ar-CH, 2C), 114.5 (Ar-CH, 2C), 1322.5 (Ar-C, 1C), 144.2 (Ar-C, 1C), 159.0 [C(O), 1C], 160.0 [C(O), 1C], 166.0 (CH, 1C).

Anal. Calcd for $C_{20}H_{31}NO_4$ (349.23): C, 68.74; H, 8.94; N, 4.01. Found: C, 69.24; H, 8.93; N, 3.86.

(3*R*,4*R*)-2-Methyl-3-(4-methylbenzenesulfonamido)-4-formylundecane (5b)

Prepared according to the general procedure with 1-octene (230 µL, 163 mg, 1.45 mmol, 4.0 equiv) and *N*-isobutylidene-4-methylbenzenesulfonamide (**6d**; 81 mg, 0.36 mmol, 1.0 equiv). Purification was achieved by flash column chromatography (cyclohexane–EtOAc, 50:1) to give **5b**.

Yield: 100 mg (0.274 mmol, 76%); colorless oil; 78% ee determined by chiral HPLC (Chiralpak-AD-H; 25 cm × 4.6 mm ID; *n*-heptane–*i*-PrOH, 85:15; 1.0 mL/min; λ = 214 nm): t_R = 6.3 (major), 6.8 (minor) min; $[\alpha]_D^{22}$ +4.3 (*c* = 1.20, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.85–0.92 (m, 9 H, CH_3), 1.14–1.40 (m, 10 H, CH_2), 1.32–1.40 (m, 2 H, CH_2), 1.56 (m_c, 1 H, CH), 2.42 (s, 3 H, CH_3), 2.43–2–47 (m, 1 H, CH), 3.48 (m_c, 1 H, CH), 3.41* (m_c, 1 H, CH), 4.85 (d, $^3J_{NH–CH}$ = 9.1 Hz, 1 H, NH), 4.97* (d, $^3J_{NH–CH}$ = 10.0 Hz, 1 H, NH), 7.28 (t, ^3J = 7.8 Hz, 2 H, *o*-Ar-H), 7.74 (t, ^3J = 8.2 Hz, 2 H, *o*-Ar-H), 9.57 (m_c, 1 H, CH), 9.48* (d, $^3J_{CH–CH}$ = 3.3 Hz, 1 H, CH). * = diastereomer.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2 (CH_3, 3C), 21.6 (CH_2, 1C), 25.8 (CH_2, 1C), 26.1 (CH, 1C), 27.8 (CH_2, 1C), 29.1 (CH_2, 1C), 29.2 (Me_{Tol}, 1C), 29.4 (CH, 1C), 29.6 (CH_2, 1C), 31.8 (CH_2, 1C), 53.7 (CH, 1C), 54.9 (CH, 1C), 127.1 (Ar-CH, 2C), 129.7 (Ar-CH, 2C), 138.5 (Ar-C, 1C), 143.4 (Ar-C, 1C), 203.9 [C(O), 1C].

Continuative Reactions

Diethyl 5-*tert*-Butoxycarbonylamino-4-heptylhex-2-enedioate (7) through Horner–Wadsworth–Emmons Reaction

To a suspension of NaH (60% in mineral oil, 3.8 mg, 96 µmol, 1.1 equiv) in CH_2Cl_2 (1 mL), ethyl (diethoxyphosphoryl)acetate (22 mg, 96 µmol, 1.1 equiv) was dropped at 0 °C and the mixture was stirred for 1 h at the same temperature. Aldehyde **4a** (30 mg, 87 µmol, 1.0 equiv) was added and the solution was stirred for 16 h at r.t. The reaction mixture was then quenched with sat. aq NH_4Cl (1 mL) and H_2O (1 mL), the phases were separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 2.5 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. Purification was achieved by flash column chromatography (cyclohexane–EtOAc, 25:1) to give **7**.

Yield: 41 mg (86 µmol, 99%); colorless oil; $[\alpha]_D^{22}$ +27.5 (*c* = 1.50, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.80 (t, $^3J_{Me–CH2}$ = 7.1 Hz, 3 H, CH_3), 1.20 (m_c, 16 H, CH_3, CH_2), 1.39 (s, 9 H, *t*-Bu), 1.42–1.57 (m, 2 H, CH_2), 2.53 (m_c, 0.8 H, CH), 2.50* (m_c, 0.2 H, CH), 4.12 (q, $^3J_{CH2–CH3}$ = 7.2 Hz, 2 H, CH_2), 4.14 (q, $^3J_{CH2–CH3}$ = 7.2 Hz, 2 H, CH_2), 4.37 (dd, $^3J_{CH–CH}$ = 4.3 Hz, $^3J_{CH–NH}$ = 9.1 Hz, 0.8 H, CH), 4.29* (m_c, 0.2 H, CH), 4.86 (d, $^3J_{NH–CH}$ = 9.1 Hz, 0.8 H, NH), 4.89* (d, $^3J_{NH–CH}$ = 9.1 Hz, 0.2 H, NH), 5.75 (dd, $^3J_{CHA–CHB}$ = 15.6 Hz, $^4J_{CHA–CH}$ = 0.9 Hz, 0.8 H, CH_A), 5.77* (dd, $^3J_{CHA–CHB}$ = 15.7 Hz, $^4J_{CHA–CH}$ = 0.9 Hz, 0.2 H, CH_A), 6.63 (dd, $^3J_{CHB–CHA}$ = 15.7 Hz, $^3J_{CHB–CH}$ = 9.5 Hz, 0.8 H, CH_B), 6.64* (dd, $^3J_{CHB–CHA}$ = 15.9 Hz, $^3J_{CHB–CH}$ = 9.7 Hz, 0.2 H, CH_B). * = diastereomer.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3, 1C), 14.3 (CH_3, 2C), 22.7 (CH_2, 1C), 27.2 (CH_2, 1C), 28.4 (CH_3, *t*-Bu, 3C), 29.1 (CH_2, 1C), 29.5 (CH_2, 1C), 30.4 (CH_2, 1C), 31.9 (CH_2, 1C), 45.5 (CH, 0.8C), 46.0* (CH, 0.2C), 56.6 (CH, 1C), 60.5 (CH_2-Ester, 2C), 123.9 (CH_A, 0.8C), 124.1* (CH_A, 0.2C), 146.8 (CH_B, 0.8C), 147.2* (CH_B, 0.2C), 155.6 [C(O), 1C], 166.0 [C(O), 1C], 171.4 [C(O), 1C]. * = diastereomer.

MS (CI, NH_3): *m*/*z* = 314.3 (53), 375.3 (100), 431.3 (61) [M + NH_3]$^+$.

HRMS (CI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{40}NO_6$ + NH_3: 431.31211; found: 431.31180 (Δ: 0.7 ppm).

General Procedure for the Wittig Olefination[10b]

Aldehyde **4a** (1.0 equiv) was dissolved in THF (0.07 M) and the corresponding phosphorous yilde (1.2–1.5 equiv) was added at r.t. The reaction mixture was stirred overnight at r.t., then the solvent was evaporated under reduced pressure and the product was purified by flash column chromatography (cyclohexane–EtOAc).

Ethyl 2-*tert*-Butoxycarbonylamino-3-(3-oxobut-1-enyl)decanoate (8)

Prepared according to the general procedure with **4a** (30 mg, 87 µmol, 1.0 equiv) and (triphenyl-l5-phosphanylidene)propan-2-one (42 mg, 0.13 mmol, 1.5 equiv) in THF–CH_2Cl_2 (1:1). Purification was achieved by flash column chromatography (cyclohexane–EtOAc, 10:1) to give **8**.

Yield: 27 mg (70 µmol, 81%); colorless oil; $[\alpha]_D^{22}$ +30.5 (*c* = 1.00, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, $^3J_{Me–CH2}$ = 7.1 Hz, 3 H, CH_3), 1.18–1.32 (m, 13 H, CH_3, CH_2), 1.43 (s, 9 H, *t*-Bu), 1.52–1.60 (m, 2 H, CH_2), 2.24 (s, 0.8 H, CH_3), 2.25* (s, 0.2 H, CH_3), 2.66 (m_c, 0.8 H, CH), 2.59* (m_c, 0.2 H, CH), 4.19 (q, $^3J_{CH2–CH3}$ = 7.2 Hz, 1.6 H, CH_2), 4.20* (q, $^3J_{CH2–CH3}$ = 7.2 Hz, 0.4 H, CH_2), 4.36–4.46 (m, 1 H, CH), 5.01 (d, $^3J_{NH–CH}$ = 8.7 Hz, 0.8 H, NH), 5.08* (d, $^3J_{NH–CH}$ = 8.7 Hz, 0.2 H, NH), 6.06 (dd, $^3J_{CHA–CHB}$ = 16.0 Hz, $^4J_{CHA–CH}$ = 0.8 Hz, 0.8 H, CH_A), 6.07* (d, $^3J_{CHA–CHB}$ = 16.0 Hz, 0.2 H, CH_A), 6.54 (dd, $^3J_{CHB–CHA}$ = 15.9 Hz, $^3J_{CHB–CH}$ = 9.4 Hz, 0.8 H, CH_B), 6.56* (dd, $^3J_{CHB–CHA}$ = 15.7 Hz, $^3J_{CHB–CH}$ = 9.4 Hz, 0.2 H, CH_B). * = diastereomer.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3, 1C), 14.3 (CH_3, 1C), 22.7 (CH_2, 1C), 26.9 (CH_2, 1C), 27.1 (CH_2, 1C), 27.2 (CH_2, 1C), 28.3 (CH_3, *t*-Bu, 3C), 29.1 (CH_2, 1C), 29.4 (CH_2, 1C), 31.8 (CH_3, 1C), 46.1 (CH, 0.8C), 46.2* (CH, 0.2C), 56.6 (CH, 1C), 61.6 (CH_2-ester, 2C), 133.1 (CH_A, 0.8C), 133.4* (CH_A, 0.2C), 146.0 (CH_B, 0.8C), 146.6* (CH_B, 0.2C), 155.5 [C(O), 1C], 171.1 [C(O), 1C], 198.1 [C(O), 1C]. * = diastereomer.

MS (CI, NH_3): *m*/*z* = 182.1 (34), 239.0 (83), 284.2 (34), 328.2 (50), 345.2 (100), 384.3 (29) [M$^+$ + H], 401.3 (30) [M$^+$ + NH_3].

HRMS (CI): *m*/*z* [M + NH_4]$^+$ calcd for $C_{21}H_{41}N_2O_5$: 401.30155; found: 401.30110 (Δ: 1.1 ppm).

1-Ethyl 8-Methyl 2-*tert*-Butoxycarbonylamino-3-heptyl-6-oxo-oct-4-enedioate (9)

Prepared according to the general procedure with **4a** (30 mg, 87 μmol, 1.0 equiv) and methyl 3-oxo-4-(triphenyl-l5-phosphanylidene)butyrate (50 mg, 0.13 mmol, 1.5 equiv). The reaction mixture was stirred at 60 °C for 6 d. Purification was achieved by flash column chromatography (cyclohexane–EtOAc, 10:1) to give **9**.

Yield: 35 mg (79 μmol, 91%); colorless oil; $[\alpha]_D^{22}$ +42.5 (*c* = 0.40, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.80 (t, $^3J_{Me–CH2}$ = 7.1 Hz, 3 H, CH_3), 1.20 (m_c, 13 H, CH_3, CH_2), 1.45 (s, 9 H, *t*-Bu), 1.52–1.67 (m, 2 H, CH_2), 2.69 (m_c, 0.8 H, CH), 2.50* (m_c, 0.2 H, CH), 3.58 (s, 2 H, CH_2), 3.70 (s, 3 H, OMe), 4.19 (q, $^3J_{CH2–CH3}$ = 7.2 Hz, 2 H, CH_2), 4.42 (m_c, 1 H, CH), 5.01 (d, $^3J_{NH–CH}$ = 9.1 Hz, 1 H, NH), 6.15 (dd, $^3J_{CHA–CHB}$ = 16.1 Hz, $^4J_{CHA–CH}$ = 0.8 Hz, 0.8 H, CH_A), 6.16* (d, $^3J_{CHA–CHB}$ = 15.7 Hz, 0.2 H, CH_A), 6.61 (dd, $^3J_{CHB–CHA}$ = 16.5 Hz, $^3J_{CHB–CH}$ = 9.4 Hz, 0.8 H, CH_B), 6.67* (dd, $^3J_{CHB–CHA}$ = 16.4 Hz, $^3J_{CHB–CH}$ = 9.4 Hz, 0.2 H, CH_B). * = diastereomer.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3, 1C), 14.3 (CH_3, 2C), 22.7 (CH_2, 1C), 27.2 (CH_2, 1C), 27.5 (CH_2, 1C), 28.4 (CH_3, *t*-Bu, 3C), 29.1 (CH_2, 1C), 29.2 (CH_2, 1C), 29.5 (CH_2, 1C), 45.9 (CH, 1C), 46.1 (CH_2, 1C), 46.9 (CH, 1C), 52.5 (OMe, 1C), 61.8 (CH_2-ester, 2C), 131.6 (CH_A, 1C), 148.0 (CH_B, 1C), 155.0 [C(O), 1C], 167.7 [C(O), 1C], 173.2 [C(O), 1C] 192.0 [C(O), 1C]. * = diastereomer.

MS (CI, NH_3): *m*/*z* = 240.2 (56), 324.2 (63), 386.2 (14), 403.2 (100), 442.2 (10) $[M^+ + H]$.

HRMS (CI): *m*/*z* $[M + NH_4]^+$ calcd for $C_{23}H_{43}N_2O_7$: 459.30703; found: 459.30750 (Δ: –1.0 ppm).

Grignard Addition Reactions; General Procedure

The Grignard reagent (1.0 M in THF, 1.4 equiv) was cooled to –78 °C and a solution of the corresponding aldehyde **4a** or **4b** (1 equiv) in Et_2O (0.5 mL) was added dropwise. The reaction mixture was maintained at –78 °C for 1 h, then warmed to r.t. over 1 h. The reaction was then quenched with sat. aq NH_4Cl and stirred for 15 min. Subsequently, the reaction mixture was acidified with aq HCl (1 M) and the layers were separated. The aqueous phase was extracted with Et_2O (3 × 3 mL) and the combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and the solvent was evaporated under reduced pressure. Purification was achieved by flash column chromatography (cyclohexane–EtOAc, 50:1→25:1).

***tert*-Butyl (4-Heptyl-2-oxo-5-methyltetrahydrofuran-3-yl)carbamate (10)**

Prepared from aldehyde **4a** (68 mg, 0.2 mmol, 1.00 equiv).

Yield: 25 mg (0.08 mmol, 40%); colorless oil; $[\alpha]_D^{22}$ –3.1 (*c* = 0.45, $CHCl_3$, 22 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, $^3J_{Me–CH2}$ = 6.7 Hz, 3 H, CH_3), 1.26 (m_c, 12 H, CH_2), 1.43 (d, $^3J_{Me–CH}$ = 6.6 Hz, 3 H, CH_3), 1.46 (s, 9 H, *t*-Bu), 2.39 (m_c, 0.9 H, CH), 4.48 (q, $^3J_{CH–CH3}$ = 6.7 Hz, 1 H, CH), 4.60 (dd, $^3J_{CH–CH}$ = 6.7 Hz, $^3J_{CH–NH}$ = 8.5 Hz, 1 H, CH), 4.90 (m_c, 0.9 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3, 1C), 20.6 (CH_3, 1C), 22.7 (CH_2, 1C), 26.8 (CH_2, 1C), 27.3 (CH_2, 1C), 28.3 (CH_2, 1C), 29.1 (CH_2, 1C), 29.6 (CH_2, 1C), 31.8 (CH_2, 1C), 44.4 (CH, 1C), 52.5 (CH, 1C), 79.9 (CH, 1C), 80.6 (*t*-Bu, 1C), 155.6 (C(O), 1C), 175.1 (C(O), 1C).

MS (CI, NH_3): *m*/*z* = 85.0 (24), 213.2 (17), 3258.2 (37), 275.2 (100), 314.3 (22) $[M + H]^+$, 331.3 (19) $[M + NH_4]^+$. Signal assignment in the NMR spectra was based on H,H- and C,H-COSY experiments. Assignment of relative configuration was based on NOESY experiments.

HRMS (CI): *m*/*z* $[M + NH_4]^+$ calcd for $C_{17}H_{35}N_2O_4$: 331.25968; found: 331.26000 (Δ: 1.0 ppm).

Benzyl (4-Heptyl-2-oxo-5-vinyltetrahydro-furan-3-yl)carbamate (11)

Prepared from aldehyde **4b** (109 mg, 0.289 mmol, 1.00 equiv) to give lactone **11**.

Yield: 64 mg (0.18 mmol, 62%); colorless oil; $[\alpha]_D^{22}$ –3.1 (*c* = 0.45, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, $^3J_{Me–CH2}$ = 6.6 Hz, 3 H, CH_3), 1.25 (m_c, 12 H, CH_2), 2.60 (m_c, 0.9 H, CH), 2.62* (m_c, 0.1 H, CH), 4.59 (dd, $^3J_{CH–CH}$ = $^3J_{CH–NH}$ = 7.2 Hz, 1 H, CH), 4.81 (m_c, 1 H, CH), 5.13 (m, 3 H, NH, CH_2), 5.28 (d, $^3J_{CH–CH}$ = 10.1 Hz, 1 H, CH), 5.37 (d, $^3J_{CH–CH}$ = 17.3 Hz, 1 H, CH), 5.90 (ddd, $^3J_{CH–CH}$ = 17.3 Hz, $^3J_{CH–CH}$ = 10.1 Hz, $^3J_{CH–CH}$ = 5.2 Hz, 1 H, CH),7.35 (m_c, 5 H, Ar-H). * = diastereomer.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3, 2C), 22.7 (CH_2, 1C), 26.7 (CH_2, 1C), 26.8 (CH_2, 1C), 29.1 (CH_2, 1C), 29.6 (CH_2, 1C), 31.8 (CH_2, 1C), 43.5 (CH, 1C), 52.6 (CH, 1C), 67.6 (CH_2, 1C), 82.3 (CH, 1C), 117.4 (CH_2, 1C), 128.2 (Ar-C, 2C), 128.5 (Ar-C, 1C), 128.7 (Ar-C, 2C), 134.5 (CH, 1C), 136.0 (Ar-C, 1C), 156.1 [C(O), 1C], 174.7 [C(O), 1C]. Signal assignment in the NMR spectra was based on H,H- and C,H-COSY experiments. Assignment of relative configuration was based on NOESY experiments.

MS (CI, NH_3): *m*/*z* = 91.1 (18), 360.2 (100) $[M^+ + H]$, 364.2 (48), 377.2 (77) $[M^+ + NH_4]$.

HRMS (CI): *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{30}NO_4$: 360.21748; found: 360.21710 (Δ: –1.1 ppm).

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Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis. Included are further experimental descriptions, determination of enantiomeric excess, and spectroscopic and analytical data.

References

(1) For recent examples, see: (a) Van Zandt, M. C.; Whitehouse, D. L.; Golebiowski, A.; Ji, M. K.; Zhang, M.; Beckett, R. P.; Jagdmann, G. E.; Ryder, T. R.; Sheeler, R.; Andreoli, M.; Conway, B.; Mahboubi, K.; D'Angelo, G.; Mitschler, A.; Cousido-Siah, A.; Ruiz, F. X.; Howard, E. I.; Podjarny, A. D.; Schroeter, H. *J. Med. Chem.* **2013**, *56*, 2568. (b) Wei, X.; Shu, C.; Haddad, N.; Zeng, X.; Patel, N. D.; Tan, Z.; Liu, J.; Lee, H.; Shen, S.; Campbell, S.; Varsolona, R. J.; Busacca, C. A.; Hossain, A.; Yee, N. K.; Senanayake, C. H. *Org. Lett.* **2013**, *15*, 1016. (c) Dunetz, J. R.; Berliner, M. A.; Xiang, Y.; Houck, T. L.; Salingue, F. H.; Chao, W.; Yuandong, C.; Shenghua, W.; Huang, Y.; Farrand, D.; Boucher, S. J.; Damon, D. B.; Makowski, T. W.; Barrila, M. T.; Chen, R.; Martínez, I. *Org. Process Res. Dev.* **2012**, *16*, 1635. (d) Fei, Z.; Kong, W.; Wang, H.; Peng, J.; Sun, F.; Yin, Y.; Bajwa, J.; Jiang, X. *Org. Process Res. Dev.* **2012**, *16*, 1436. (e) Henry, S. S.; Brady, M. D.; Laird, D. L. T.; Rubie, J. C.; Varie, D. L.; Monn, J. A. *Org. Lett.* **2012**, *14*, 2662. (f) Li, T.; Liang, J.; Ambrogelly, A.; Brennan, T.; Gloor, G.; Huisman, G.; Lalonde, J.; Lekhal, A.; Mijts, B.; Muley, S.; Newman, L.; Tobin, M.; Wong, G.; Zaks, A.; Zhang, X. *J. Am. Chem. Soc.* **2012**, *134*, 6467. (g) Khantikaew, I.; Takahashi, M.; Kumamoto, T.; Suzuki, N.; Ishikawa, T. *Tetrahedron* **2012**, *68*, 878. (h) LeTiran, A.; Stables, J. P.; Kohn, H. *Bioorg. Med. Chem.* **2001**, 2693.

(2) For a review, see: *Asymmetric Synthesis and Application of α-Amino Acids*, In *ACS Symposium Series*; Vol. 1009; Soloshonok, V. A.; Izawa, K., Eds.; American Chemical Society: Washington DC, **2009**, DOI: 10.1021/bk-2009-1009.
(3) (a) Nash, A.; Soheili, A.; Tamber, U. K. *Org. Lett.* **2013**, *15*, 4770. (b) Follmann, M.; Gaul, F.; Schäfer, T.; Kopec, S.; Hamley, P. *Synlett* **2005**, 1009.
(4) (a) Gorges, J.; Ullrich, A.; Kazmaier, U. *Eur. J. Org. Chem.* **2013**, 4372. (b) Becker, D.; Kazmaier, U. *J. Org. Chem.* **2013**, *78*, 59. (c) Deska, J.; Kazmaier, U. *Angew. Chem. Int. Ed.* **2007**, *46*, 4570; *Angew. Chem.* **2007**, *119*, 4654. (d) Hudlicky, T.; Oppong, K.; Duan, C.; Stanton, C.; Laufersweiler, M. J.; Natchus, M. G. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 627.
(5) For reviews on organocatalysis of the Mannich reaction, see: (a) Ting, A.; Schaus, S. E. *Eur. J. Org. Chem.* **2007**, 5797. (b) Marques, M. M. B. *Angew. Chem. Int. Ed.* **2006**, *45*, 348; *Angew. Chem.* **2006**, *118*, 356.
(6) (a) List, B. *J. Am. Chem. Soc.* **2000**, *122*, 9336. (b) List, B.; Pojarliev, P.; Biller, W. T.; Martin, H. J. *J. Am. Chem. Soc.* **2002**, *124*, 827. (c) Notz, W.; Saakthivel, K.; Bui, T.; Zhong, G.; Barbas, C. F. III *Tetrahedron Lett.* **2001**, *42*, 199. (d) Córdova, A.; Watanabe, S.; Tanaka, F.; Notz, W.; Barbas, C. F. III *J. Am. Chem. Soc.* **2002**, *124*, 1866. (e) Hayashi, Y.; Tsuboi, W.; Ashimine, I.; Urushima, T.; Shoji, M.; Sakai, K. *Angew. Chem. Int. Ed.* **2003**, *42*, 3677; *Angew. Chem.* **2003**, *115*, 3805 . (f) Córdova, A. *Chem. Eur. J.* **2004**, *10*, 1987. (g) Enders, D.; Grondal, C.; Vrettou, M. *Synthesis* **2006**, 3597. (h) Yang, J. W.; Stadtler, M.; List, B. *Angew. Chem. Int. Ed.* **2007**, *46*, 609; *Angew. Chem.* **2007**, *119*, 615. (i) Vesely, J.; Rios, R.; Ibrahem, I.; Córdova, A. *Tetrahedron Lett.* **2007**, *48*, 421.
(7) Gianelli, C.; Sambri, L.; Carlone, A.; Bartoli, G.; Melchiorre, P. *Angew. Chem. Int. Ed.* **2008**, *47*, 8700; *Angew. Chem.* **2008**, *120*, 8828.
(8) Abillard, O.; Breit, B. *Adv. Synth. Catal.* **2007**, 1891.
(9) Fuchs, D.; Nasr-Esfahani, M.; Diab, L.; Šmejkal, T.; Breit, B. *Synlett* **2013**, 1657.
(10) For other tandem reactions applying hydroformylation as the initial step, see: (a) Eilbracht, P.; Bärfacker, L.; Buss, C.; Hollmann, C.; Kitsos-Rzychon, B. E.; Kranemann, C. L.; Rische, T.; Roggenbuck, R.; Schmidt, A. *Chem. Rev.* **1999**, *99*, 3329. (b) Breit, B.; Zahn, S. K. *Angew. Chem. Int. Ed.* **1999**, *38*, 969; *Angew. Chem.* **1999**, *111*, 1022. (c) Zahn, S. K.; Breit, B. *Angew. Chem. Int. Ed.* **2001**, *40*, 1910; *Angew. Chem.* **2001**, *113*, 1964. (d) Köhling, P.; Schmidt, A. M.; Eilbracht, P. *Org Lett.* **2003**, *5*, 3213. (e) Chercheja, S.; Nadakudity, S. K.; Eilbracht, P. *Adv. Synth. Catal.* **2010**, *352*, 637. (f) Chercheja, S.; Rothenbücher, T.; Eilbracht, P. *Adv. Synth. Catal.* **2009**, *351*, 339. (g) Stiller, J.; Vorholt, A. J.; Ostrowski, K. A.; Behr, A.; Christmann, M. *Chem. Eur. J.* **2012**, *18*, 9496. (h) Takahashi, K.; Yamashita, M.; Ichihara, T.; Nakano, K.; Nozaki, K. *Angew. Chem. Int. Ed.* **2010**, *49*, 4488; Angew. Chem. 2010, 122, 4590.
(11) (a) Breit, B.; Seiche, W. *J. Am. Chem. Soc.* **2003**, *125*, 6608; 6-DPPon is commercially available from Aldrich. (b) Gellrich, U.; Huang, J.; Seiche, W.; Keller, M.; Meuwly, M.; Breit, B. *J. Am. Chem. Soc.* **2011**, *122*, 964. (c) Huang, J.; Häussinger, D.; Gellrich, U.; Seiche, W.; Breit, B.; Meuwly, M. *J. Phys. Chem. B* **2012**, *116*, 14406. (d) Gellrich, U.; Seiche, W.; Keller, M.; Breit, B. *Angew. Chem. Int. Ed.* **2012**, *51*, 11033; *Angew. Chem.* **2012**, *124*, 11195. (e) Gellrich, U.; Himmel, D.; Meuwly, M.; Breit, B. *Chem. Eur. J.* **2013**, *19*, 16272. (f) Fuchs, D.; Rousseau, G.; Diab, L.; Gellrich, U.; Breit, B. *Angew. Chem. Int. Ed.* **2012**, *51*, 2178; *Angew. Chem.* **2012**, *124*, 2220. (g) Agabekov, V.; Breit, B. *Chem. Sci.* **2013**, *4*, 2418.
(12) Seiche, W.; Schuschkowski, A.; Breit, B. *Adv. Synth. Catal.* **2005**, *347*, 1488.
(13) Straub, A. T.; Otto, M.; Usui, I.; Breit, B. *Adv. Synth. Catal.* **2013**, *355*, 2071.
(14) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(15) Gottlieb, H. E.; Kotlyar, V.; Nudelman, A. *J. Org. Chem.* **1997**, *62*, 7512.
(16) Makio, H.; Fujita, T. *Macromol. Rapid Commun.* **2007**, *28*, 698.
(17) Brown, H. C.; Lynch, G. J. *J. Org. Chem.* **1981**, *46*, 531.
(18) Rawat, V.; Chouthaiwale, P. V.; Suryavanshi, G.; Sudalai, A. *Tetrahedron: Asymmetry* **2009**, *20*, 2173.
(19) Magdziak, D.; Lalic, G.; Lee, H. M.; Fortner, K. C.; Aloise, A. D.; Shair, M. D. *J. Am. Chem. Soc.* **2005**, *127*, 7284.
(20) Kemme, S. T.; Šmejkal, T.; Breit, B. *Adv. Synth. Catal.* **2008**, *350*, 989.
(21) Schleicher, K. D.; Jamison, T. F. *Org. Lett.* **2007**, *9*, 875.
(22) Tsuzki, Y.; Chiba, K.; Mizuno, K.; Tomita, K.; Suzuki, K. *Tetrahedron: Asymmetry* **2001**, *12*, 2989.
(23) Nagano, T.; Kinoshita, H. *Bull. Chem. Soc. Jpn.* **2000**, *73*, 1605.
(24) Manhas, M. S.; Ghosh, M.; Bose, A. K. *J. Org. Chem.* **1990**, *55*, 575.
(25) Chemla, F.; Hebbe, V.; Normant, J.-F. *Synthesis* **2000**, 75.

