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Article

Fatty Acid and Amino Acid Derivatives in Organocatalyzed Michael Additions

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Abstract

Amino acid derivatives, such as β-keto esters and pyrrolones, were used as nucleophiles in organocatalyzed Michael additions to nitroalkene acceptors, while fatty acid derivatives acted as both nucleophiles (β-keto esters) and electrophile (nitroalkene acceptor). Bifunctional noncovalent organocatalysts were employed as asymmetric organocatalysts. Twenty compounds – including fatty acid and amino acid derivatives, as well as fatty acid–amino acid conjugates – were prepared with enantioselectivities of up to 98% *ee*. All novel products were fully characterized. This research demonstrates the ease of assembling readily available fatty acid and amino acid building blocks under ambient conditions.

Keywords: fatty a cids; a mino a cids; β-keto e sters; p yrrolones; n itroalkene a cceptors; M ichael addition; asymmetric organocatalysis; enantioselectivity; diastereoselectivity; tetronic acid

1. Introduction

The enantioselective construction of carbon–carbon and carbon–heteroatom bonds in modern organic synthesis is crucial, as enantiomerically pure compounds play a key role in natural products and pharmaceuticals. Asymmetric organocatalysis, the third pillar of enantioselective catalysis, is a powerful tool that enables the formation of complex products from simple building blocks in an asymmetric manner, without the use of potentially toxic metals and under mild, often non-inert reaction conditions [1,2]. Among numerous organocatalyzed transformations, the asymmetric 1,4-addition to electron-deficient alkenes stands out as a key reaction, serving as a platform for organocatalyst development, the formation of advanced, functionalized, enantiomerically pure building blocks, and target-oriented asymmetric synthesis [3–8]. Even after nearly 20 years of intensive research on asymmetric organocatalyzed 1,4-additions, the reaction remains relevant and is applied to various new nucleophile–electrophile starting building blocks [9–20].

While various amino acid derivatives, such as β-keto esters [21,22], pyrrolones [22–24], azlactones [25–27], glycine Schiff bases [28–31], α,β-unsaturated amino acids [32], α-aryl-α-isocyano acetates [33], α-amino acid-derived thiazolones [34], 1*H*-imidazol-4(5*H*)-ones [35], α-imino esters [36], and others, have been used as building blocks in asymmetric organocatalyzed transformations, only a few fatty acid building blocks have been reported in asymmetric organocatalysis. Among the few reports, the enantioselective organocatalytic synthesis of 3-hydroxy fatty acids and fatty γ-lactones is notable [37,38]. Bifunctional phosphorus-based organocatalysts have been used for the atom-economical reaction of CO_2 with epoxidized oleochemicals [39], while amines and alkanolamines as organocatalysts have been used in the amidation of fatty acid methyl esters with 3-(dimethylamino)-1-propylamine [40]. Because fatty acid derivatives exhibit various biological activities, including antitumor [41] and antiproliferative activity [42], inhibition of glioma cell growth [43], activity as inhibitors against Gram-positive *Staphylococcus aureus* [44], and serving as biomarkers of oxidative stress [45], the demand for simple and efficient enantioselective syntheses – including

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organocatalytic methods – of fatty acid derivatives continues to grow. On the other hand, nitro fatty acids are an emerging class of bioactive fatty acids [46–53].

We report the synthesis of readily available β-keto ester derivatives of fatty acids and amino acids [22], as well as amino acid-derived pyrrolones used as nucleophiles in the (asymmetric) organocatalyzed Michael addition to fatty acid-derived nitroalkene and *trans*-β-nitrostyrene [22]. These reactions yield a small library of fatty acid and amino acid derivatives, doubly fatty acid derivatives, and amino acid–fatty acid conjugates. The results highlight the ease of forming these potentially interesting product classes, as well as the drawbacks and challenges encountered.

2. Results and Discussion

Synthesis. β-Keto ester nucleophiles were prepared by Masamune-Claisen homologation of carboxylic acids (Scheme 1) [22]. Activation of Boc-protected glycine **1a**, Boc-protected β-alanine **1b**, glycolic acid derivative **1c**, and palmitic acid (**1d**), stearic acid (**1e**), and linoleic acid (**1f**) with 1,1'-carbonyldiimidazole (CDI) in anhydrous THF, followed by addition of alkyl (methyl, *tert*-butyl) potassium malonate in the presence of magnesium chloride, afforded the corresponding β-keto esters **2a–g** in 45–91% yield. Except for compound **2f**, the other β-keto esters are known in the literature and are individually referenced in the Experimental section. β-Keto esters **2h** and **2i** were prepared in three and five steps, respectively, from H-Orn(Boc)-OMe·HCl (**3**). Amidation of **3** with stearic acid (**1e**) gave amido ester **4**, which was hydrolyzed under basic conditions to acid **5** and then homologated to β-keto ester **2h** in 44% yield over three steps. For the preparation of **2i**, compound **4** was Boc-deprotected using TFA to give ammonium salt **6**, followed by amidation with stearic acid (**1e**) to yield diamido ester **7**. Hydrolysis of **7** furnished acid **8**, which was transformed into β-keto ester **2i** in 20% yield over five steps (Scheme 1). Compounds **6–8** and **2i** have low solubility in most solvents, including chloroform and dimethyl sulfoxide. Solubility in chloroform increases significantly with the addition of small amounts of trifluoroacetic acid (700 µL $CHCl_3$ and 20 µL TFA to dissolve 10–20 mg of above mentioned compounds).

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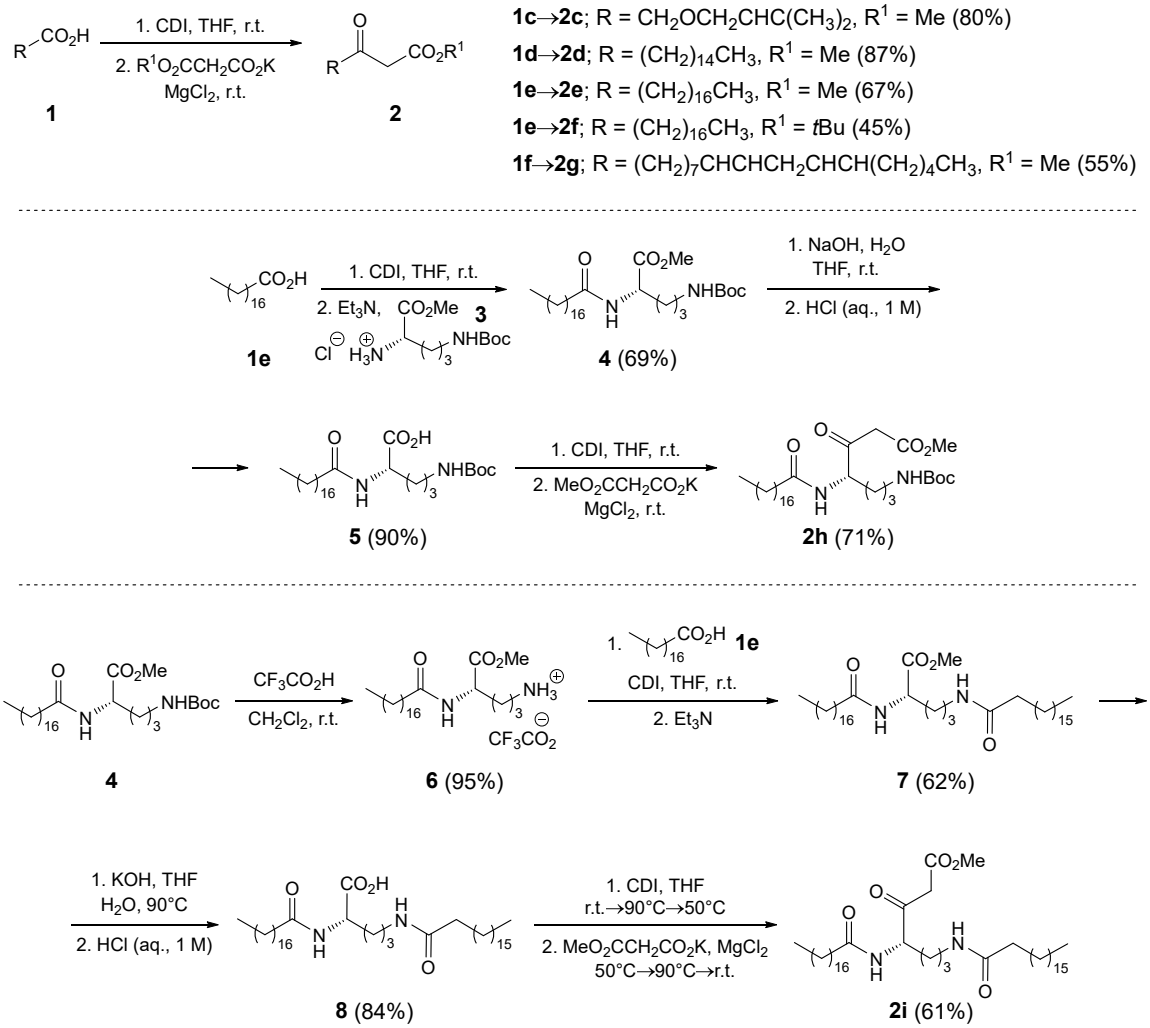

Scheme 1. Synthesis of β-keto ester building blocks **2a–i**.

Similarly, the pyrrolone nucleophiles **11a–c** were prepared from appropriately protected phenylalanine **9a**, ornithine **9b**, and glutamic acid **9c** in a two-step procedure (Scheme 2) [22,23]. Initial homologation to the corresponding β-keto esters **10a–c** was followed by treatment with *N*,*N*-dimethylformamide dimethyl acetal at elevated temperature, yielding the corresponding pyrrolones **11a–c** in 57–62% yield after two steps. All attempts to prepare the corresponding pyrrolone **11d** from amido β-keto ester **2h** resulted in complex product mixtures (Scheme 2). In addition to commercially available *trans*-β-nitrostyrene (**12**), fatty acid-derived nitroalkene electrophile **16** was prepared in four steps from palmitic acid (**1d**) following procedures described in the literature [54–56]. Reduction of palmitic acid (**1d**) with $LiAlH_4$ gave alcohol **13**, which was oxidized with pyridinium chlorochromate (PCC) to aldehyde **14**. The Henry reaction with nitromethane in the presence of *t*BuOK afforded β-nitro alcohol **15**, which was dehydrated after treatment with trifluoroacetic anhydride (TFAA) and Et_3N at –10°C to nitroalkene **16** in 38% yield over four steps (Scheme 2).

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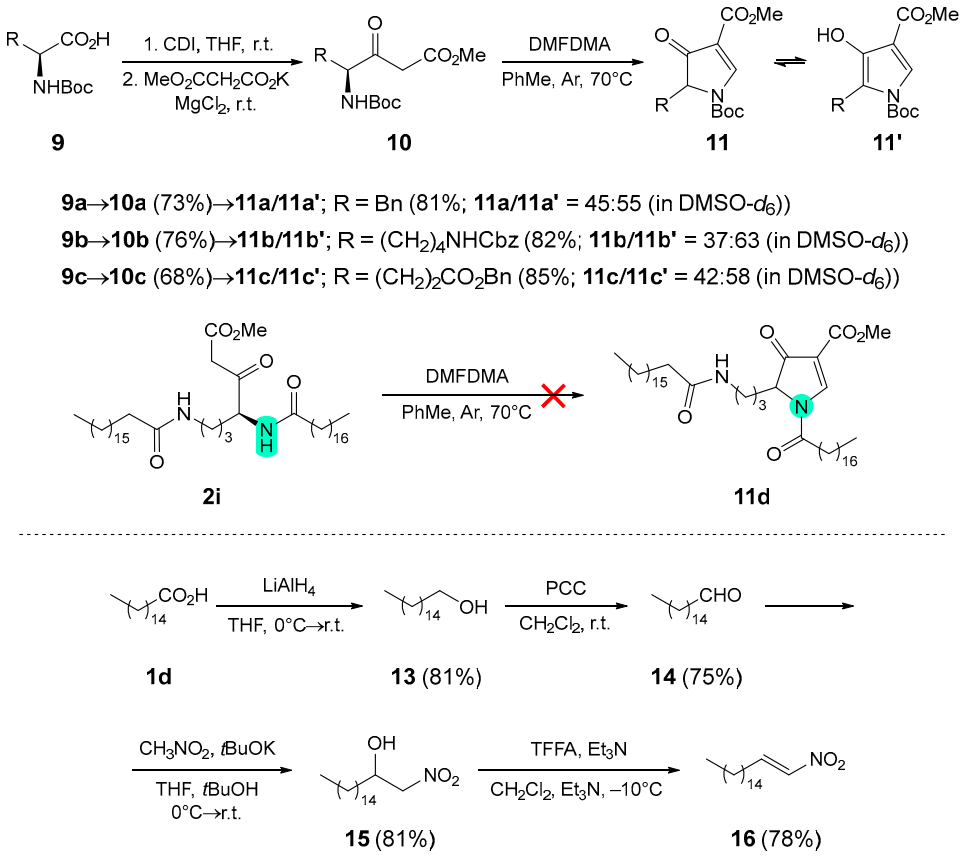

Scheme 2. Synthesis of the starting building blocks: pyrrolones **11a–c** and the fatty acid-derived nitroalkene **16**.

Next, the organocatalyzed 1,4-addition of Boc-β-alanine-derived β-keto ester **2b** to *trans*-β-nitrostyrene (**12**), yielding adduct **17b**, was used as a model reaction for catalyst optimization (Scheme 3) [21]. Noncovalent bifunctional organocatalysts **I–IX** (see ESI, Scheme S1) were tested, and achiral organocatalyst **X** was used to prepare the racemic product ***rac*-17b**. The best results for enantioselectivity, conversion, and reaction profile were obtained with the (+)-cinchonine-derived squaramide catalyst **VIII** (100% conversion, 85% yield, 95% *ee* for both diastereomers, (1*R*)-enantioselectivity), followed by the camphor-derived squaramide catalyst **I**, which showed the best complementary enantioselectivity (100% conversion, 92% and 93% *ee* for both diastereomers, (1*S*)-enantioselectivity). Screening of solvents (toluene, THF, EtOAc, MeCN) revealed broad compatibility of the model reaction catalyzed by **VIII** (*ee* between 94% and 96%), except for MeOH (81% and 83% *ee*) (Scheme 3; for details, see ESI, Scheme S2).

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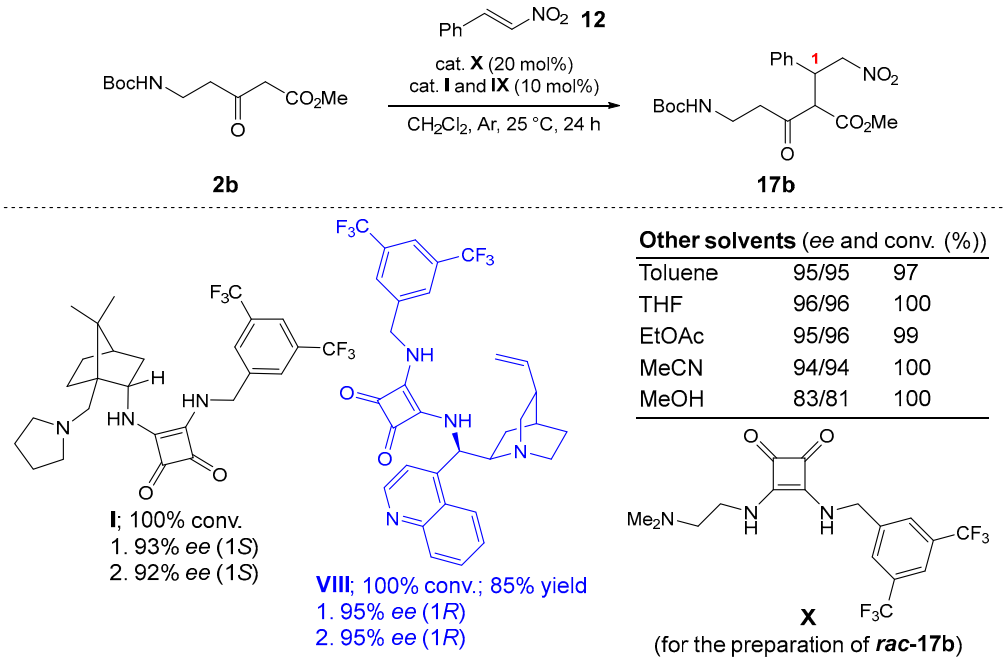

Scheme 3. Organocatalyst and solvent optimization for the addition of Boc-β-alanine-derived β-keto ester **2b** to *trans*-β-nitrostyrene (**12**). **2b** (0.3 mmol), **12** (0.2 mmol), cat. **I** and **VIII** (10 mol%), anhydrous CH_2Cl_2 (1.0 mL), 25 °C, Ar, 24 h. Catalyst **X** was used to prepare ***rac*-17b**.

With optimal reaction conditions established (organocatalyst **VIII**, dichloromethane, 25 °C), the scope of the organocatalyzed 1,4-additions of β-keto esters **2** to *trans*-β-nitrostyrene (**12**) and fatty acid-derived nitroalkene **16** was explored. The achiral bifunctional noncovalent organocatalyst **X** was used efficiently to prepare all racemic adducts ***rac*-17a–l** in 37–88% yield. All doubly fatty acid-derived products ***rac*-17g,i,k** as well as products ***rac*-17c** and ***rac*-17e**, could not be separated by chiral HPLC. Only the racemic products ***rac*-17a,b,d,f,h,j,l** for which all four stereoisomers (two pairs of racemic diastereomers) were separated on a chiral HPLC column, were resynthesized using chiral noncovalent bifunctional organocatalyst **VIII** (Scheme 4); the corresponding chiral nonracemic products **17a,b,d,f,h,j,l** were obtained in 47–89% yield, with high enantioselectivity (91–98% *ee*) and diastereoselectivity ranging from 50:50 to 64:36. Lastly, chiral nonracemic β-keto esters **2h** and **2i** were used for addition to *trans*-β-nitrostyrene (**12**) and fatty acid-derived nitroalkene **16**. With the achiral organocatalyst **X**, addition of **2h** to *trans*-β-nitrostyrene (**12**) and **16** gave the desired products **17m** (71% yield) and **17n** (77% yield), respectively, each as an inseparable mixture of four diastereomers in 27:21:24:28 and 26:28:25:21 ratios, respectively. Similarly, addition of **2i** to **12** and **16** gave the desired products **17o** (29% yield) and **17p** (25% yield), respectively, each as an inseparable mixture of four diastereomers in 24:22:30:24 and 25:25:27:23 ratios, respectively. Application of chiral quinuclidine catalyst **VIII** for the synthesis of products **17n** and **17p** improved the diastereomer ratio, yielding compound **17n** in 88% yield with a 45:11:8:36 diastereomer ratio and compound **17p** in 23% yield with a 39:11:12:38 diastereomer ratio (Scheme 4). No attempts have been made to determine the diastereomeric or enantiomeric ratios of compounds **17m–n** by HPLC. The stereochemical integrity (enantiomer ratio) of the starting β-keto esters **2h** and **2i** was not verified; nevertheless, this transformation highlights the challenges encountered – diastereoselectivity and separation of stereomers – in this simple, inherently diastereoselective reaction.

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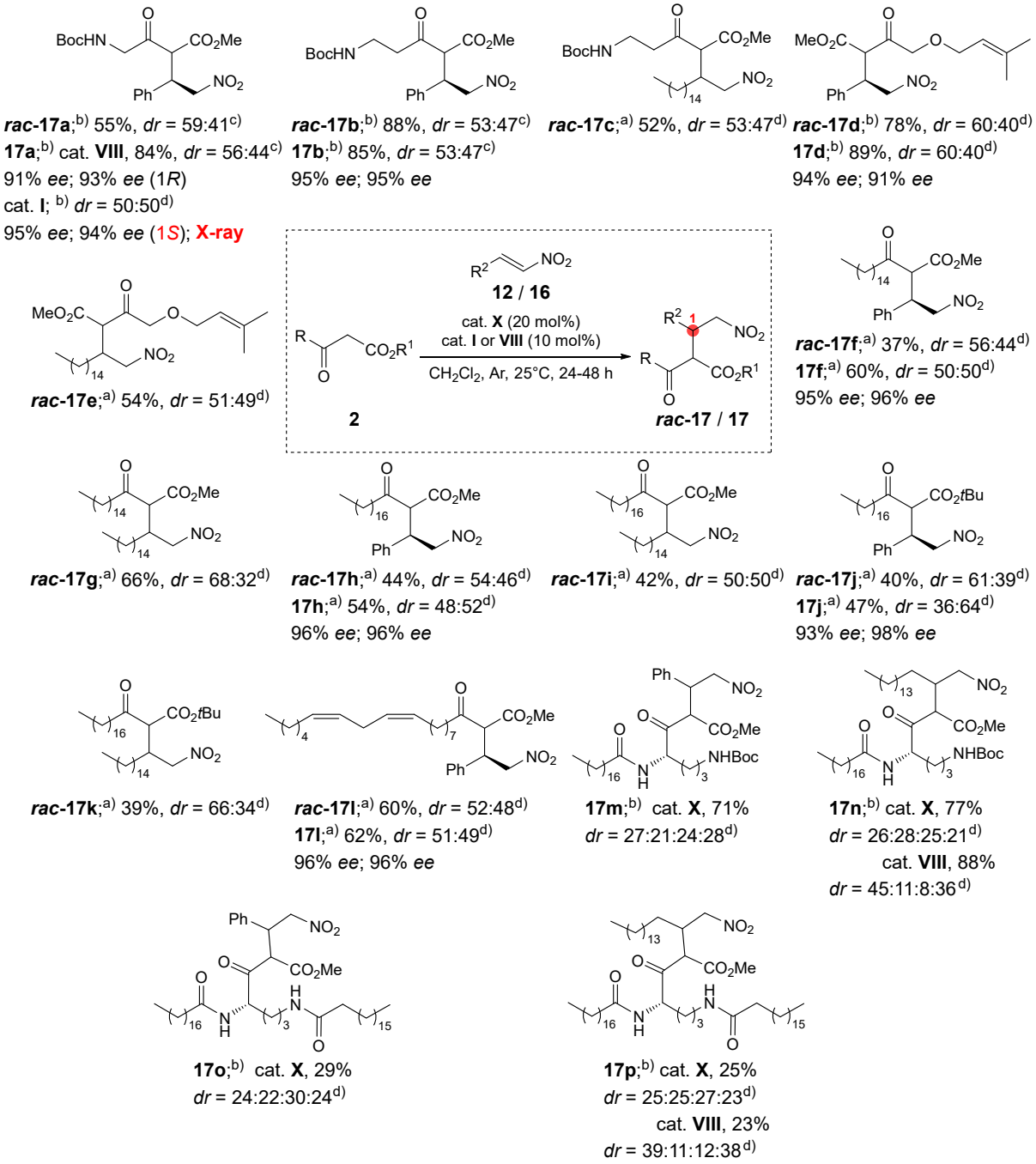

Scheme 4. Scope for the addition of β-keto ester **2** to *trans*-β-nitrostyrene (**12**) and fatty acid-derived nitroalkene **16**; if not stated otherwise, organocatalyst **VIII** was used, yielding (1*R*)-enantioselectivity. Catalyst **X** was used to prepare the racemic products ***rac*-17a–l**. [a] **2** (0.3 mmol), **12** or **16** (0.2 mmol), cat. **X** (20 mol%), **I** (10 mol%), and **VIII** (10 mol%), anhydrous CH_2Cl_2 (1.0 mL), 25 °C, Ar, 24–48 h. [b] **2** (0.2 mmol), **12** or **16** (0.3 mmol), cat. **X** (20 mol%), **I** (10 mol%), and **VIII** (10 mmol%), anhydrous CH_2Cl_2 (1.0 mL), 25 °C, Ar, 24–48 h. [c] In DMSO-d_6. [d] In $CDCl_3$.

Next, phenylalanine- **11a**, ornithine- **11b**, and glutamic acid-derived pyrrolones **11c** were tested as nucleophiles in the organocatalyzed addition to fatty acid nitroalkene **16** (Scheme 5). Reactions with racemic catalyst **X** proceeded smoothly, yielding the corresponding products ***rac*-18a–c** in 65–77% yields with high diastereoselectivity, ranging from 90:10 to 97:3. Application of the camphor-derived organocatalyst **I** in anhydrous toluene at room temperature, which were the optimal catalyst and conditions in our previous organocatalyzed additions of pyrrolone nucleophiles to nitroalkene acceptors [23], gave the corresponding chiral products **18a–c** in 18–69% yield. For the phenylalanine-

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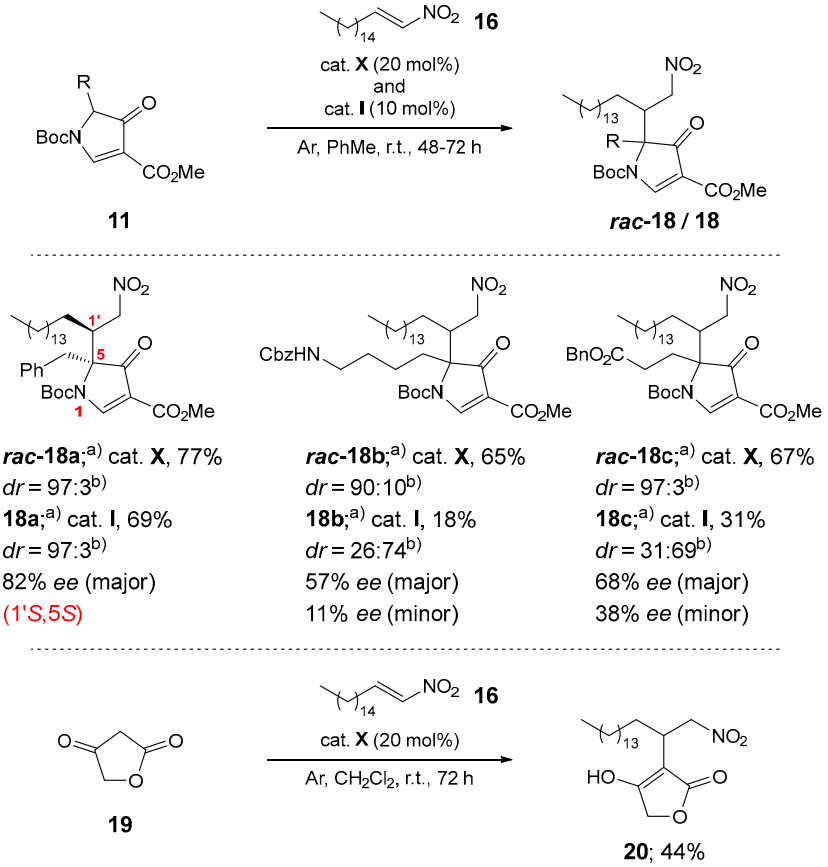
derived product **18a** (69% yield), the diastereoselectivity remained unchanged at 97:3, with an enantioselectivity of 82% *ee* for the major diastereomer. For the ornithine-derived adduct **18b** and the glutamic acid-derived adduct **18c**, the diastereoselectivity with organocatalyst **I** not only decreased significantly but also reversed, changing from 90:10 to 26:74 for **18b** and from 97:3 to 31:69 for **18c**. For both diastereomers of product **11b**, enantioselectivity could only be tentatively determined due to partial overlap (57% *ee* for the major diastereomer and 11% *ee* for the minor diastereomer). Similarly, for product **18c**, enantioselectivity was 68% *ee* for the major diastereomer and 38% *ee* for the minor diastereomer. Finally, tetronic acid (**19**) was used as a nucleophile in the addition to nitroalkene **16**, yielding the expected product **20** in 44% yield. All attempts to separate the stereoisomers of product **20** were unsuccessful (Scheme 5).



Scheme 5. Scope for the addition of pyrrolones **11** and tetronic acid (**19**) to fatty acid-derived nitroalkene **16**. [a] **11** or **19** (0.3 mmol), **16** (0.2 mmol), cat. **X** (20 mol%) or **I** (10 mol%), anhydrous PhMe or CH_2Cl_2 (1.0 mL), 25 °C, Ar, 48–72 h. [b] In $CDCl_3$.

Structure determination. The structures of novel compounds **2f**, **2h**, **2i**, **4**–**8**, **16**–**18**, and **20** were confirmed by spectroscopic methods (^{1}H and ^{13}C NMR, IR, and high-resolution mass spectrometry), while compound **15** was used as a crude product for further transformations; its structure was confirmed by ^{1}H NMR. The diastereomers of compounds **17**/***rac*-17**, **18**/***rac*-18**, and **20** could not be separated by column chromatography and were characterized as mixtures of diastereomers. The diastereomeric ratios of compounds **17**/***rac*-17** and **18**/***rac*-18** were determined by proton spectra, in which the non-overlapping signals were integrated. Similarly, the keto-enol ratios of compounds **2**, **10**, **11**, **17**/***rac*-17**, and **20** were determined from proton spectra. β-Keto esters **2**, **10**, and **17**/***rac*-17** contain up to 17% (17% for compound **2i**, see ESI) of the enol form, as indicated by the enol signal in the proton spectra (a singlet) at approximately 11.5–13.5 ppm. For details, see the ESI. In contrast, the enol form is the predominant tautomer for the pyrrolones **11a–c** in DMSO-d_6 (ranging from 55% for **11a'** to 63% for **11b'**; see Scheme 2) [22,23]. The tetronic acid derivative **20** exists in $CDCl_3$ solution exclusively in the enol form, as indicated by the enol-ester resonances in the ^{13}C NMR spectra at 99.1

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ppm, 177.4 ppm, and 177.9 ppm, and by the absence of a ketone signal above 200 ppm (see Scheme 5 and the ESI). The (*E*) configuration around the C=C bond of compound **16** was assigned based on the vicinal R**H**C=C**H**NO_2 coupling constant (^3J = 13.4 Hz). The structure and (1*S*,2*S*)-absolute configuration of the stereoisomer of adduct **17a** (prepared with organocatalyst **I**) were determined by single-crystal X-ray diffraction analysis (Figure 1). The (1*S*)-absolute configuration is consistent with our previous findings [21]. Based on this, we assigned the (1*R*)-absolute configuration to the major enantiomer of both diastereomers of products **17a**, **17b**, **17d**, **17f**, **17h**, **17j**, and **17l** prepared with organocatalyst **VIII**. The absolute configuration at the C-2 chiral center is labile due to rapid keto-enol tautomerization. The (1'*S*,5*S*)-absolute configuration of the major diastereomer of product **18a** (see Scheme 5) was assigned based on our previous results in the series of 1,4-adducts of pyrrolones to nitroalkene acceptors [22].

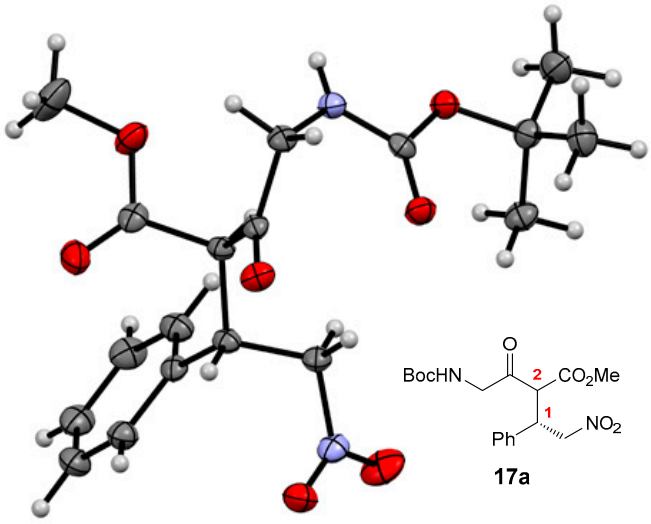

Figure 1. Molecular structure of the (1*S*,2*S*)-stereoisomer of product **17a**, synthesized using catalyst **I**. Thermal ellipsoids are shown at 50% probability.

4. Materials and Methods

Solvents for extractions and chromatography were of technical grade and were distilled prior to use. Extracts were dried over technical grade anhydrous Na_2SO_4. Melting points were determined on a Kofler micro hot stage and on SRS OptiMelt MPA100 – Automated Melting Point System (Stanford Research Systems, Sunnyvale, California, United States). The NMR spectra were obtained on a Bruker UltraShield 500 plus spektrometer and on a BRUKER AVANCE NEO 600 MHz NMR spektrometer (Bruker, Billerica, Massachusetts, United States) at 500 and 600 MHz for ^{1}H and 126 and 150 MHz for ^{13}C nucleus, respectively, using DMSO-d_6 and $CDCl_3$ with TMS as the internal standard, as solvents. Mass spectra were recorded on an Agilent 6224 Accurate Mass TOF LC/MS and Agilent 6530 Q-TOF LC/MS coupled with Agilent 1260 Infinity2 HPLC (Agilent Technologies, Santa Clara, California, United States), IR spectra on a Perkin-Elmer Spectrum BX FTIR spectrophotometer (PerkinElmer, Waltham, Massachusetts, United States). Column chromatography (CC) was performed on silica gel (Silica gel 60, particle size: 0.035-0.070 mm (Sigma-Aldrich, St. Louis, Missouri, United States)). HPLC analyses were performed on an Agilent 1260 Infinity LC (Agilent Technologies, Santa Clara, California, United States) using CHIRALPAK IA-3 (0.46 cm ø × 25 cm), CHIRALPAK AD-H (0.46 cm ø × 25 cm), CHIRALCEL OD-H (0.46 cm ø × 25 cm), and CHIRALPAK AS-H (0.46 cm ø × 25 cm) as chiral column (CHIRAL TECHNOLOGIES, INC., West Chester, Pennsylvania, United States). All the

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commercially available chemicals used were purchased from Sigma-Aldrich (St. Louis, Missouri, United States).

Organocatalysts **I** [21], **II** [57], **III** [58], **IV** [58], **VI** [59], **VII** [60], **VIII** [61], and **IX** [62] were prepared following the literature procedures; organocatalyst **V** was purchased from Sigma-Aldrich.

Synthesis of β-keto esters 2 from carboxylic acids 1 – General procedure 1 (GP1)

To a solution or suspension of carboxylic acid **1** (10 mmol) in anhydrous THF (50 mL), 1,1'-carbonyldiimidazole (CDI; 12 mmol, ω = 0.97, 1.672 g) was added under argon, and the resulting reaction mixture was stirred for 2 h at room temperature. A solid mixture of $MgCl_2$ (9.8 mmol, ω = 0.98, 952 mg) and methyl potassium malonate (15 mmol, 2.343 g) or *tert*-butyl potassium malonate (15 mmol, ω = 0.95, 3.130 g) was then added. The reaction mixture was stirred for a further 24 hours under argon at room temperature. The volatiles were evaporated *in vacuo*, the residue was dissolved in EtOAc (150 mL) and washed with $NaHSO_4$ (1 M in H_2O, 3×50 mL), $NaHCO_3$ (aq. sat., 2×20 mL), and NaCl (aq. sat., 2×50 mL). The organic phase was dried over anhydrous Na_2SO_4, filtered, and the volatiles evaporated *in vacuo*. If necessary, the residue was purified by column chromatography (CC, Silica gel 60). The fractions containing the product were combined and the volatiles were evaporated *in vacuo*.

Synthesis of methyl 4-((tert-butoxycarbonyl)amino)-3-oxobutanoate (2a) [22]

Following *GP1*. Prepared from (*tert*-butoxycarbonyl)glycine (**1a**) (10 mmol, 1.752 g), methyl potassium malonate (15 mmol, 2.343 g); isolation by extraction. Yield: 2.10 g (9.1 mmol, 91 %) of yellowish oil. ^{1}H-NMR (500 MHz, DMSO-d_6): δ 1.39 (*s*, 9H), 3.60 (*s*, 2H), 3.63 (*s*, 3H), 3.86 (*d*, *J*=5.9 Hz, 2H), 7.13 (*t*, *J*=5.9 Hz, 1H). ^{13}C-NMR (126 MHz, DMSO-d_6): δ 28.18, 45.91, 49.81, 51.93, 78.30, 155.81, 167.50, 200.67.

*Synthesis of methyl 5-((*tert*-butoxycarbonyl)amino)-3-oxopentanoate (**2b**) [22]*

Following *GP1*, prepared from Boc-β-alanine (**1b**) (10 mmol, 1.892 g), methyl potassium malonate (15 mmol, 2.343 g); isolation by extraction. Yield: 2.18 g (8.9 mmol, 89 %) of yellowish oil. ^{1}H-NMR (500 MHz, DMSO-d_6): δ 1.36 (*s*, 9H), 2.66 (*t*, *J*=6.9 Hz, 2H), 3.11 (*q*, *J*=6.9 Hz, 2H), 3.61 (*s*, 2H), 3.62 (*s*, 3H), 6.77 (*t*, *J*=5.6 Hz, 1H). ^{13}C-NMR (126 MHz, DMSO-d_6): δ 28.24, 34.88, 42.40, 48.68, 51.84, 77.72, 155.53, 167.71, 202.42.

*Synthesis of methyl 4-((3-methylbut-2-en-1-yl)oxy)-3-oxobutanoate (**2c**) [63]*

Following *GP1*. Prepared from 2-((3-methylbut-2-en-1-yl)oxy)acetic acid (**1c**) [64] (10 mmol, 1.442 g), methyl potassium malonate (15 mmol, 2.343 g); isolation by extraction. Yield: 1.602 g (8.0 mmol, 80 %) of colorless oil. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.69 (*s*, 3H), 1.77 (*s*, 3H), 3.55 (*s*, 2H), 3.74 (*s*, 3H), 4.04 (*d*, *J*=7.1 Hz, 2H), 4.09 (*s*, 2H), 5.29 – 5.36 (*m*, 1H). ^{13}C-NMR (126 MHz, $CDCl_3$): δ 18.11, 25.88, 45.77, 52.41, 67.89, 74.63, 119.97, 138.70, 167.62, 202.30.

*Synthesis of methyl 3-oxooctadecanoate (**2d**) [65]*

Following *GP1*. Prepared from palmitic acid (**1d**) (10 mmol, 2.564 g), methyl potassium malonate (15 mmol, 2.343 g); isolation by extraction and column chromatography (EtOAc/petroleum ether = 1:10). Yield: 2,717 g (8.70 mmol, 87 %) of white solid; m.p. = 49.2–50.5 °C. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.88 (*t*, *J*=6.9 Hz, 3H), 1.19 – 1.35 (*m*, 24H), 1.53 – 1.65 (*m*, 2H), 2.53 (*t*, *J*=7.4 Hz, 2H), 3.45 (*s*, 2H), 3.74 (*s*, 3H). ^{13}C-NMR (126 MHz, $CDCl_3$): δ 14.26, 22.83, 23.60, 29.14, 29.49, 29.50, 29.58, 29.73, 29.77, 29.79, 29.80, 29.82, 29.83, 32.06, 43.23, 49.15, 52.46, 167.85, 203.01.

*Synthesis of methyl 3-oxoicosanoate (**2e**) [65]*

Following *GP1*. Prepared from stearic acid (**1e**) (10 mmol, 2.845 g), methyl potassium malonate (15 mmol, 2.343 g); isolation by extraction and column chromatography (EtOAc/petroleum ether =

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1:10). Yield: 2.282 g (6.70 mmol, 67 %) of white solid; m.p. = 49.5 –51.2 °C. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.88 (*t*, *J*=6.9 Hz, 3H), 1.18 – 1.34 (*m*, 28H), 1.55 – 1.63 (*m*, 2H), 2.53 (*t*, *J*=7.4 Hz, 2H), 3.45 (*s*, 2H), 3.74 (*s*, 3H). ^{13}C-NMR (151 MHz, $CDCl_3$): δ 14.25, 22.83, 23.60, 29.14, 29.49, 29.50, 29.58, 29.73, 29.78, 29.79, 29.80, 29.83, 32.06, 43.22, 49.14, 52.45, 167.84, 203.00 (3 signals missing due to overlapping).

Synthesis of tert*-butyl 3-oxoicosanoate (**2f**)*

Following *GP1*. Prepared from stearic acid (**1e**) (10 mmol, 2.845 g), *tert*-butyl potassium malonate (15 mmol, ω = 0.95, 3.130 g); isolation by extraction and column chromatography (EtOAc/petroleum ether = 1:15). Yield: 1.722 g (4.50 mmol, 45 %) of white solid; m.p. = 36.9–38.1 °C. EI-HRMS: *m*/*z* = 327.2885 (MH^+-*t*BuOH); $C_{20}H_{39}O_3$ requires: *m*/*z* = 327.2894 (MH^+-*t*BuOH); ν_{max} 2960, 2916, 2849, 1729, 1715, 1466, 1406, 1367, 1329, 1276, 1260, 1155, 1131, 1109, 1080, 947, 920, 842, 790, 723, 647 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.88 (*t*, *J*=6.9 Hz, 3H), 1.21 – 1.34 (*m*, 28H), 1.47 (*s*, 9H), 1.55 – 1.61 (*m*, 2H), 2.51 (*t*, *J*=7.4 Hz, 2H), 3.34 (*s*, 2H). ^{13}C-NMR (151 MHz, $CDCl_3$): δ 14.26, 22.83, 23.62, 28.10, 29.21, 29.50, 29.52, 29.59, 29.74, 29.78, 29.80, 29.81, 29.84, 32.07, 43.09, 50.81, 81.99, 166.69, 203.68 (3 signals missing due to overlapping).

*Synthesis of methyl (11Z,14Z)-3-oxoicosa-11,14-dienoate (**2g**) [65]*

Following *GP1*. Prepared from linoleic acid (**1f**) (10 mmol, 2.804 g), methyl potassium malonate (15 mmol, 2.343 g); isolation by extraction and column chromatography (EtOAc/petroleum ether = 1:5). Yield: 1.851 g (5.50 mmol, 55 %) of colorless oil. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.89 (*t*, *J*=6.9 Hz, 3H), 1.23 – 1.40 (*m*, 14H), 1.54 – 1.64 (*m*, 2H), 1.97 – 2.09 (*m*, 4H), 2.53 (*t*, *J*=7.4 Hz, 2H), 2.77 (*t*, *J*=6.6 Hz, 2H), 3.45 (*s*, 2H), 3.74 (*s*, 3H), 5.28 – 5.43 (*m*, 4H). ^{13}C-NMR (126 MHz, $CDCl_3$): δ 14.21, 22.71, 23.57, 25.76, 27.31, 27.33, 29.10, 29.21, 29.39, 29.48, 29.72, 31.66, 43.20, 49.15, 52.46, 128.02, 128.19, 130.15, 130.35, 167.83, 202.95.

*Synthesis of methyl (S)-4-((*tert*-butoxycarbonyl)amino)-3-oxo-5-phenylpentanoate (**10a**) [22]*

Following *GP1*. Prepared from Boc-L-phenylalanine (**9a**) (10 mmol, 2.653 g), methyl potassium malonate (15 mmol, 2.343 g); isolation by extraction. Yield: 2.346 g (7.30 mmol, 73 %) of colorless oil. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.40 (*s*, 9H), 2.98 (*dd*, *J*=7.5, 14.1 Hz, 1H), 3.14 (*dd*, *J*=6.2, 14.1 Hz, 1H), 3.46 (*d*, *J*=16.0 Hz, 1H), 3.52 (*d*, *J*=16.0 Hz, 1H), 3.71 (*s*, 3H), 4.56 (*q*, *J*=7.2 Hz, 1H), 4.96 – 5.07 (*m*, 1H), 7.14 – 7.20 (*m*, 2H), 7.21 – 7.35 (*m*, 3H).

*Synthesis of methyl (S)-8-(((benzyloxy)carbonyl)amino)-4-((*tert*-butoxycarbonyl)amino)-3-oxooctanoate (**10b**) [22]*

Following *GP1*. Prepared from Boc-Lys(Z)-OH (**9b**) (10 mmol, 3.804 g), methyl potassium malonate (15 mmol, 2.343 g); isolation by extraction. Yield: 3.317 g (7.60 mmol, 76 %) of colorless oil. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.30 – 1.65 (*m*, 5H), 1.43 (*s*, 9H), 1.81 – 1.93 (*m*, 1H), 3.12 – 3.27 (*m*, 2H), 3.54 (*d*, *J*=15.7 Hz, 1H), 3.59 (*d*, *J*=16.0 Hz, 1H), 3.73 (*s*, 3H), 4.27 – 4.36 (*m*, 1H), 4.93 (*t*, *J*=6.0 Hz, 1H), 5.05 – 5.17 (*m*, 2H), 5.27 (br *d*, *J*=7.7 Hz, 1H), 7.28 – 7.39 (*m*, 5H).

*Synthesis of 7-benzyl 1-methyl (S)-4-((*tert*-butoxycarbonyl)amino)-3-oxoheptanedioate (**10c**) [23]*

Following *GP1*. Prepared from Boc-Glu(OBzl)-OH (**9c**) (10 mmol, 3.374g), methyl potassium malonate (15 mmol, 2.343 g); isolation by extraction. Yield: 2.675 g (6.80 mmol, 68 %) of colorless oil. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.43 (*s*, 9H), 1.80 – 1.91 (*m*, 1H), 2.22 – 2.32 (*m*, 1H), 2.38 – 2.56 (*m*, 2H), 3.55 – 3.65 (*m*, 2H), 3.73 (*s*, 3H), 4.38 – 4.45 (*m*, 1H), 5.12 (*s*, 2H), 5.23 (br *d*, *J*=8.1 Hz, 1H), 7.29 – 7.41 (*m*, 5H).

*Synthesis of methyl (S)-5-((*tert*-butoxycarbonyl)amino)-2-stearamidopentanoate (**4**)*

To a solution of stearic acid (**1e**) (20 mmol, 5.690 g) in anhydrous THF (50 mL) was added 1,1′-carbonyldiimidazole (CDI; 22 mmol, ω = 0.97, 3.678 g) under argon and the resulting reaction mixture

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was stirred for 2 h at room temperature. Then H-Orn(Boc)-OMe×HCl (**3**) (22 mmol, ω = 0.96, 6.480 g) and Et_3N (22 mmol, 3.07 mL) were added. The reaction mixture was stirred for a further 24 hours under argon at room temperature. The volatiles were evaporated *in vacuo*, the residue was dissolved in CH_2Cl_2 (150 mL) and washed with $NaHSO_4$ (1 M in H_2O, 4×50 mL), $NaHCO_3$ (aq. sat., 3×20 mL) and NaCl (aq. sat., 2×50 mL). The organic phase was dried over anhydrous Na_2SO_4, filtered and the volatiles evaporated *in vacuo*. Yield: 7.076 g (13.8 mmol, 69 %) of white solid; m.p. = 86.0–88.0 °C. EI-HRMS: *m/z* = 513.4272 (MH^+); $C_{29}H_{57}N_2O_5$ requires: *m/z* = 513.4262 (MH^+); ν_{max} 3345, 2915, 2847, 1762, 1684, 1648, 1526, 1473, 1462, 1369, 1285, 1252, 1212, 1171, 1143, 1047, 994, 950, 871, 754, 729, 719, 654 cm^{-1}. ^{1}H-NMR (500 MHz, DMSO-d_6): δ 0.85 (*t*, *J*=6.8 Hz, 3H), 1.14 – 1.31 (*m*, 30H), 1.37 (*s*, 9H), 1.42 – 1.57 (*m*, 3H), 1.61 – 1.69 (*m*, 1H), 2.09 (*t*, *J*=7.1 Hz, 2H), 2.89 (*q*, *J*=6.8 Hz, 2H), 3.60 (*s*, 3H), 4.14 – 4.23 (*m*, 1H), 6.79 (*t*, *J*=5.7 Hz, 1H), 8.14 (*d*, *J*=7.5 Hz, 1H). ^{13}C-NMR (126 MHz, DMSO-d_6): δ 13.98, 22.11, 25.23, 26.02, 28.20, 28.26, 28.55, 28.72, 28.78, 28.97, 29.02, 29.05, 31.31, 34.94, 51.65, 51.70, 77.40, 155.58, 172.43, 172.78 (7 signals missing due to overlapping).

*Synthesis of (S)-5-((tert-butoxycarbonyl)amino)-2-stearamidopentanoic acid (**5**)*

To a solution/suspension of methyl (*S*)-5-((*tert*-butoxycarbonyl)amino)-2-stearamidopentanoate (**4**) (1.70 mmol, 872 mg) in a mixture of H_2O (3.0 mL) and THF (3.0 mL) was added NaOH (15.0 mmol, 600 mg). The reaction mixture was stirred for 3 hours at room temperature. The mixture was acidified with HCl (aq. 1 M) to pH < 3 and extracted with EtOAc (3×30 mL). The combined organic layers were washed with brine (1×10 mL), dried over Na_2SO_4, filtered and the volatiles evaporated *in vacuo*. The residue was azeotropically evaporated with $CHCl_3$ (3×30 mL) to give the anhydrous product **5**. Yield: 763 mg (1.53 mmol, 90 %) of white solid; m.p. = 82.0–84.3 °C. EI-HRMS: *m/z* = 499.4113 (MH^+); $C_{28}H_{55}N_2O_5$ requires: *m/z* = 499.4105 (MH^+); ν_{max} 3359, 2955, 2916, 2849, 1738, 1682, 1605, 1525, 1465, 1454, 1388, 1365, 1290, 1274, 1244, 1210, 1170, 1112, 1043, 1019, 957, 890, 860, 783, 727, 637 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.88 (*t*, *J*=6.9 Hz, 3H), 1.17 – 1.36 (*m*, 28H), 1.44 (*s*, 9H), 1.52 – 1.67 (*m*, 4H), 1.68 – 1.79 (*m*, 1H), 1.87 – 1.98 (*m*, 1H), 2.25 (*t*, *J*=7.8 Hz, 2H), 3.04 – 3.27 (*m*, 2H), 4.60 (*td*, *J*=4.9, 7.5 Hz, 1H), 4.86 (*t*, *J*=6.4 Hz, 1H), 6.73 (br *d*, *J*=7.4 Hz, 1H), 9.64 (br *s*, 1H). ^{13}C-NMR (126 MHz, $CDCl_3$): δ 14.27, 22.84, 25.79, 26.56, 28.52, 29.06, 29.42, 29.49, 29.51, 29.67, 29.80, 29.83, 29.86, 32.07, 36.57, 39.88, 52.22, 79.99, 156.91, 174.55, 174.80 (5 signals missing due to overlapping). ^{1}H-NMR (500 MHz, DMSO-d_6): δ 0.85 (*t*, *J*=6.9 Hz, 3H), 1.06 – 1.31 (*m*, 29H), 1.37 (*s*, 9H), 1.32 – 1.56 (*m*, 4H), 1.61 – 1.71 (*m*, 1H), 2.04 – 2.15 (*m*, 2H), 2.84 – 2.94 (*m*, 2H), 4.13 (*td*, *J*=5.0, 8.5 Hz, 1H), 6.77 (*t*, *J*=5.8 Hz, 1H), 7.98 (*d*, *J*=7.8 Hz, 1H), 12.40 (br *s*, 1H). ^{13}C-NMR (126 MHz, DMSO-d_6): δ 13.91, 22.06, 25.24, 26.15, 28.23, 28.43, 28.57, 28.66, 28.77, 28.93, 28.97, 29.00, 31.26, 35.02, 51.54, 77.33, 155.54, 172.23, 173.71 (7 signals missing due to overlapping).

*Synthesis of methyl (S)-7-((tert-butoxycarbonyl)amino)-3-oxo-4-stearamidoheptanoate (**2h**)*

Following *GP1*, prepared from (*S*)-5-((*tert*-butoxycarbonyl)amino)-2-stearamidopentanoic acid (**5**) (1.5 mmol, 748 mg), CDI (1.8 mmol, ω = 0.97, 301 mg), $MgCl_2$ (1.47 mmol, ω = 0.98, 143 mg), methyl potassium malonate (2.25 mmol, 351 mg); isolation by extraction and column chromatography (EtOAc/petroleum ether = 1:1). Yield: 591 mg (1.065 mmol, 71 %) of white solid; m.p. = 62.3–64.9 °C. EI-HRMS: *m/z* = 555.4384 (MH^+); $C_{31}H_{59}N_2O_6$ requires: *m/z* = 555.4368 (MH^+); ν_{max} 3341, 2915, 2848, 1747, 1711, 1681, 1638, 1524, 1438, 1390, 1365, 1316, 1251, 1168, 1016, 886, 769, 719, 643 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.88 (*t*, *J*=6.9 Hz, 3H), 1.18 – 1.35 (*m*, 28H), 1.44 (*s*, 9H), 1.47 – 1.68 (*m*, 5H), 1.90 – 2.00 (*m*, 1H), 2.21 – 2.26 (*m*, 2H), 3.15 (*q*, *J*=6.7 Hz, 2H), 3.58 (*s*, 2H), 3.74 (*s*, 3H), 4.66 (br *s*, 1H), 4.68 – 4.74 (*m*, 1H), 6.43 (br *d*, *J*=7.4 Hz, 1H). ^{13}C-NMR (126 MHz, $CDCl_3$): δ 14.27, 22.83, 25.73, 26.44, 27.58, 28.52, 29.44, 29.47, 29.50, 29.63, 29.77, 29.80, 29.84, 32.06, 36.62, 39.87, 46.26, 52.66, 58.11, 79.56, 156.40, 167.45, 173.54, 201.86 (6 signals missing due to overlapping). ^{1}H-NMR (500 MHz, DMSO-d_6): δ 0.85 (*t*, *J*=6.9 Hz, 3H), 1.08 – 1.30 (*m*, 29H), 1.37 (*s*, 9H), 1.31 – 1.54 (*m*, 4H), 1.62 – 1.75 (*m*, 1H), 2.12 (*t*, *J*=7.4 Hz, 2H), 2.89 (*q*, *J*=6.2 Hz, 2H), 3.58 (*s*, 2H), 3.61 (*s*, 3H), 4.23 (*ddd*, *J*=4.5, 7.3, 9.5 Hz, 1H), 6.78 (*t*, *J*=5.9 Hz, 1H), 8.16 (*d*, *J*=7.4 Hz, 1H). ^{13}C-NMR (126 MHz, DMSO-d_6): δ 13.90, 22.05, 25.10, 25.88, 26.25, 28.22,

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28.57, 28.65, 28.71, 28.89, 28.96, 28.99, 31.25, 34.91, 45.49, 51.76, 57.75, 77.36, 155.57, 167.46, 172.67, 202.73 (7 signals missing due to overlapping).

*Synthesis of (S)-5-methoxy-5-oxo-4-stearamidopentan-1-aminium 2,2,2-trifluoroacetate (**6**)*

Methyl (*S*)-5-((*tert*-butoxycarbonyl)amino)-2-stearamidopentanoate (**4**) (10 mmol, 5.128 g) was dissolved in a 1:1 mixture of CF_3COOH and anhydrous CH_2Cl_2 (60 mL) under argon, and the reaction mixture was stirred for 3 hours at room temperature. Volatile components were evaporated *in vacuo*, and the residue was azeotropically evaporated with anhydrous toluene (3×100 mL) to give ammonium salt **6**. Yield: 5.00 g (9.50 mmol, 95%) of white solid; m.p. = 93.0–95.7 °C. EI-HRMS: *m*/*z* = 413.3726 (MH^+); $C_{24}H_{49}N_2O_3^+$ requires: *m*/*z* = 413.3738 (MH^+); ν_{max} 3318, 2915, 2848, 1752, 1671, 1645, 1528, 1474, 1462, 1430, 1400, 1381, 1358, 1276, 1237, 1207, 1173, 1127, 1067, 1003, 970, 955, 893, 839, 800, 768, 747, 723, 668, 613 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$ (700 µL) + TFA (20 µL)): δ 0.88 (*t*, *J*=6.9 Hz, 3H), 1.09 – 1.35 (*m*, 26H), 1.53 – 1.63 (*m*, 2H), 1.69 – 1.85 (*m*, 3H), 1.91 – 2.01 (*m*, 1H), 2.23 – 2.33 (*m*, 2H), 3.01 – 3.20 (*m*, 2H), 3.76 (*s*, 3H), 4.48 – 4.57 (*m*, 1H), 6.86 (*d*, *J*=7.5 Hz, 1H), 7.61 (br *s*, 3H). ^{13}C-NMR (126 MHz, $CDCl_3$ (700 µL) + TFA (20 µL)): δ 14.25, 22.84, 23.37, 25.78, 29.22, 29.28, 29.31, 29.51, 29.59, 29.74, 29.80, 29.81, 29.86, 32.07, 36.22, 39.62, 51.65, 53.08, 115.46 (*q*, *J*=287.8 Hz), 161.08 (*q*, *J*=39.3 Hz), 172.10, 176.30 (3 signals missing due to overlapping).

*Synthesis of methyl (S)-2,5-distearamidopentanoate (**7**)*

To a solution of stearic acid (**1e**) (8.5 mmol, 2.416 g) in anhydrous THF (30 mL), 1,1'-carbonyldiimidazole (CDI; 9.35 mmol, ω = 0.97, 1.563 g) was added under argon, and the resulting reaction mixture was stirred for 2 h at room temperature. The resulting activated acid was transferred to a suspension of (*S*)-5-methoxy-5-oxo-4-stearamidopentan-1-aminium 2,2,2-trifluoroacetate (**6**) (9.35 mmol, 4.924 g) in anhydrous THF (30 mL) under argon. Et_3N (9.35 mmol, 1.303 mL) was then added to the reaction mixture at room temperature. The reaction mixture was stirred at 40 °C for 12 hours. Volatile components were evaporated *in vacuo*. The residue was extracted with CH_2Cl_2 (100 mL), EtOAc (100 mL), Et_2O (100 mL), and *n*-hexane (100 mL) using a laboratory ultrasonic bath (5 minutes each), followed by decanting, respectively, to remove unreacted starting material and small portions of the product. H_2O (150 mL) was added to the residue, followed by ultrasonic bath treatment (15 minutes). The resulting precipitate was collected by filtration and thoroughly washed with H_2O (3×70 mL). The residue was dried under high vacuum at 40 °C for 12 hours to give product **7**. Yield: 3.476 g (5.270 mmol, 62 %) of white solid; m.p. = 106.7–108.4 °C. EI-HRMS: *m*/*z* = 679.6336 (MH^+); $C_{42}H_{83}N_2O_4$ requires: *m*/*z* = 679.6347 (MH^+); ν_{max} 3305, 2914, 2848, 1742, 1639, 1542, 1470, 1420, 1385, 1277, 1259, 1239, 1205, 1173, 980, 717 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$ (700 µL) + TFA (20 µL)): δ 0.88 (*t*, *J*=6.9 Hz, 6H), 1.18 – 1.36 (*m*, 56H), 1.54 – 1.77 (*m*, 7H), 1.87 – 1.97 (*m*, 1H), 2.26 – 2.38 (*m*, 4H), 3.23 – 3.34 (m, 1H), 3.34 – 3.47 (*m*, 1H), 3.79 (*s*, 3H), 4.57 – 4.64 (*m*, 1H), 6.70 (*t*, *J*=6.1 Hz, 1H), 6.79 (*d*, *J*=7.7 Hz, 1H). ^{13}C-NMR (126 MHz, $CDCl_3$ (700 µL) + TFA (20 µL)): δ 14.25, 22.84, 24.97, 25.87, 25.99, 29.20, 29.23, 29.28, 29.51, 29.56, 29.72, 29.78, 29.81, 29.83, 29.85, 30.00, 32.07, 36.28, 36.35, 39.58, 52.17, 53.15, 172.43, 176.50, 177.11 (17 signals missing due to overlapping).

*Synthesis of (S)-2,5-distearamidopentanoic acid (**8**)*

To a suspension of methyl (*S*)-2,5-distearamidopentanoate (**7**) (5 mmol, 3.393 g) in a mixture of H_2O (20 mL) and THF (5 mL), KOH (powder for synthesis, 50 mmol, 2.810 g) was added, and the reaction mixture was stirred at 90 °C for 12 hours. The mixture was cooled to room temperature, and HCl (aq., 2 M) was added under stirring until the pH reached 1–2. The precipitate was collected by filtration and thoroughly washed with H_2O (3×100 mL). The residue was dried under high vacuum at 40 °C for 12 hours to give acid **8**. Yield: 2.792 g (4.20 mmol, 84 %) of white solid; m.p. = 108.8–110.1 °C. EI-HRMS: *m*/*z* = 665.6191 (MH^+); $C_{41}H_{81}N_2O_4$ requires: *m*/*z* = 665.6191 (MH^+); ν_{max} 3310, 2955, 2916, 2849, 1736, 1639, 1586, 1545, 1466, 1446, 1418, 1372, 1275, 1245, 1211, 1181, 1128, 970, 829, 720, 685, 633 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$ (700 µL) + TFA (20 µL)): δ 0.88 (*t*, *J*=6.8 Hz, 6H), 1.09 – 1.40 (*m*, 56H),

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1.52 – 1.73 (*m*, 6H), 1.75 – 1.89 (*m*, 1H), 1.92 – 2.11 (*m*, 1H), 2.27 – 2.45 (*m*, 4H), 3.13 – 3.49 (*m*, 2H), 4.61 (*q*, *J*=6.7, 1H), 6.87 (*s*, 1H), 6.98 (*d*, *J*=7.3 Hz, 1H), 11.12 (br *s*, 1H). ^{13}C-NMR (126 MHz, $CDCl_3$ (700 µL) + TFA (20 µL)): δ 14.26, 22.84, 24.97, 25.88, 25.96, 29.14, 29.19, 29.21, 29.25, 29.27, 29.52, 29.55, 29.57, 29.73, 29.79, 29.82, 29.84, 29.86, 32.08, 36.09, 36.13, 39.82, 52.36, 175.92, 177.30, 177.72 (15 signals missing due to overlapping).

*Synthesis of methyl (S)-3-oxo-4,7-distearamidoheptanoate (**2i**)*

To a suspension of (*S*)-2,5-distearamidopentanoic acid (**8**) (2.5 mmol, 1.662 g) in anhydrous THF (25 mL), 1,1'-carbonyldiimidazole (CDI; 5 mmol, ω = 0.97, 836 mg) was added under argon, and the reaction mixture was stirred for 15 minutes at room temperature, 30 minutes at 90 °C, and 60 minutes at 50 °C. Then, a solid mixture of $MgCl_2$ (2.5 mmol, ω = 0.98, 243 mg) and methyl potassium malonate (7.5 mmol, 1.171 g) was carefully added at 50 °C. The reaction mixture was stirred for 15 minutes at 50 °C, 30 minutes at 90 °C, and 24 hours at room temperature. The volatiles were evaporated *in vacuo*, and $NaHSO_4$ (1 M in H_2O, 100 mL) was added to the residue. The mixture was stirred at room temperature for 30 minutes. The precipitate was collected by filtration and thoroughly washed with H_2O (3×100 mL). The residue was dried under high vacuum at 40 °C for 12 hours to give β-keto ester **2i**. Yield: 1.099 g (1.525 mmol, 61 %) of white solid; m.p. = 92.1–94.7 °C. EI-HRMS: *m*/*z* = 721.6456 (MH^+); $C_{44}H_{85}N_2O_5$ requires: *m*/*z* = 721.6453 (MH^+); ν_{max} 3306, 2916, 2849, 1748, 1717, 1638, 1539, 1463, 1378, 1328, 1258, 1239, 1223, 1204, 1147, 1013, 719 cm^{-1}. ^{1}H-NMR (600 MHz, $CDCl_3$): δ 0.88 (*t*, *J*=6.9 Hz, 6H), 1.18 – 1.39 (*m*, 56H), 1.51 – 1.67 (*m*, 7H), 1.88 – 1.97 (*m*, 1H), 2.17 (*t*, *J*=7.7 Hz, 2H), 2.25 (*t*, *J*=7.7 Hz, 2H), 3.22 – 3.38 (*m*, 2H), 3.58 (*d*, *J*=1.7 Hz, 2H), 3.74 (*s*, 3H), 4.65 – 4.72 (*m*, 1H), 5.87 (*t*, *J*=6.0 Hz, 1H), 6.67 (*d*, *J*=7.5 Hz, 1H). ^{13}C-NMR (151 MHz, $CDCl_3$): δ 14.26, 22.83, 25.72, 25.94, 25.98, 27.70, 29.45, 29.50, 29.52, 29.66, 29.78, 29.80, 29.81, 29.85, 32.07, 36.56, 36.96, 38.86, 46.22, 52.66, 58.21, 167.58, 173.81, 173.95, 201.90 (19 signals missing due to overlapping).

*Synthesis of pyrrolones **11** from β-keto esters **10** – General procedure 2 (GP2)*

To a solution of β-keto ester **10** (1.0 mmol) in anhydrous toluene (5 mL), DMFDMA (3 mmol, ω = 0.94, 424 µL) was added under argon and the resulting reaction mixture was stirred at 70 °C under argon until completion of the reaction, as judged by TLC analysis (1–3 hours). The volatiles were evaporated *in vacuo* and the residue was purified as quickly as possible by column chromatography (CC, Silica gel 60). The fractions containing the product **11** were combined and the volatiles were evaporated *in vacuo*. The product was immediately used for the following transformation or/and stored under argon at –20 °C.

*Synthesis of 1-(*tert*-butyl) 3-methyl 5-benzyl-4-oxo-4,5-dihydro-1*H*-pyrrole-1,3-dicarboxylate (**11a**) and 1-(*tert*-butyl) 3-methyl 5-benzyl-4-hydroxy-1*H*-pyrrole-1,3-dicarboxylate (**11a'**) [22]*

Following *GP2*. Prepared from methyl (*S*)-4-((*tert*-butoxycarbonyl)amino)-3-oxo-5-phenylpentanoate (**10a**) (1 mmol, 321.4 mg), 45 minutes; CC (EtOAc/petroleum ether = 1:1). **11a**/**11a'** = 45:55 (in DMSO-d_6). Yield: 268 mg (0.81 mmol, 81 %) of colorless oil. ^{1}H-NMR (500 MHz, DMSO-d_6) for **11a**: δ 1.55 (*s*, 9H), 3.22 (*dd*, *J*=2.7, 13.8 Hz, 1H), 3.38 (*dd*, *J*=6.4, 13.8 Hz, 1H), 3.61 (*s*, 3H), 4.58 (*dd*, *J*=2.6, 6.3 Hz, 1H), 6.91 – 6.97 (*m*, 2H), 8.71 (*s*, 1H). ^{1}H-NMR (500 MHz, DMSO-d_6) for **11a'**: δ 1.34 (*s*, 9H), 3.76 (*s*, 3H), 4.14 (*s*, 2H), 6.98 – 7.04 (*m*, 2H), 7.11 – 7.28 (*m*, 3H), 7.57 (*s*, 1H), 8.26 (*s*, 1H).

*Synthesis of 1-(*tert*-butyl) 3-methyl 5-(4-(((benzyloxy)carbonyl)amino)butyl)-4-oxo-4,5-dihydro-1*H*-pyrrole-1,3-dicarboxylate (**11b**) and 1-(*tert*-butyl) 3-methyl 5-(4-(((benzyloxy)carbonyl)amino)butyl)-4-hydroxy-1*H*-pyrrole-1,3-dicarboxylate (**11b'**) [22]*

Following *GP2*. Prepared from methyl (*S*)-8-(((benzyloxy)carbonyl)amino)-4-((*tert*-butoxycarbonyl)amino)-3-oxooctanoate (**10b**) (1 mmol, 436.5 mg), 1 hour; CC (EtOAc/petroleum ether = 1:1). **11b**/**11b'** = 37:63 (in DMSO-d_6). Yield: 336 mg (0.82 mmol, 82 %) of colorless oil. ^{1}H-NMR (500 MHz, DMSO-d_6) for **11b**: δ 0.98 – 1.08 (*m*, 1H), 1.08 – 1.19 (*m*, 1H), 1.50 (*s*, 9H), 1.83 – 1.93 (*m*, 1H),

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1.97 – 2.08 (*m*, 1H), 2.93 (*q*, *J*=6.7 Hz, 2H), 3.68 (*s*, 3H), 4.30 (*dd*, *J*=3.1, 6.5 Hz, 1H), 8.98 (*s*, 1H). ^{1}H-NMR (500 MHz, DMSO-d_6) for **11b'**: δ 1.28 – 1.46 (*m*, 4H), 1.54 (*s*, 9H), 2.70 (*t*, *J*=6.9 Hz, 2H), 2.98 (*q*, *J*=6.3 Hz, 2H), 3.73 (*s*, 3H), 4.99 (*s*, 2H), 7.23 (*t*, *J*=5.8 Hz, 1H), 7.26 – 7.41 (*m*, 5H), 7.49 (*s*, 1H), 7.95 (*s*, 1H).

*Synthesis of 1-(*tert*-butyl) 3-methyl 5-(3-(benzyloxy)-3-oxopropyl)-4-oxo-4,5-dihydro-1*H*-pyrrole-1,3-dicarboxylate (**11c**) and 1-(*tert*-butyl) 3-methyl 5-(3-(benzyloxy)-3-oxopropyl)-4-hydroxy-1*H*-pyrrole-1,3-dicarboxylate (**11c'**) [23]*

Following *GP2*. Prepared from 7-benzyl 1-methyl (*S*)-4-((*tert*-butoxycarbonyl)amino)-3-oxoheptanedioate (**10c**) (1 mmol, 393.4 mg), 45 minutes; CC (EtOAc/petroleum ether = 1:1). **11c**/**11c'** = 42:58 (in DMSO-d_6). Yield: 343 mg (0.85 mmol, 85 %) of colorless oil. ^{1}H-NMR (500 MHz, DMSO-d_6) for **11c**: δ 1.50 (*s*, 9H), 3.68 (*s*, 3H), 4.35 – 4.40 (*m*, 1H), 5.06 (*d*, *J*=5.4 Hz, 2H), 8.92 (*s*, 1H). ^{1}H-NMR (500 MHz, DMSO-d_6) for **11c'**: δ 1.53 (*s*, 9H), 2.51 – 2.57 (*m*, 2H), 2.99 – 3.05 (*m*, 2H), 3.73 (*s*, 3H), 5.08 (*s*, 2H), 7.30 – 7.40 (*m*, 5H), 7.49 (*s*, 1H), 8.11 (*s*, 1H).

*Synthesis of hexadecan-1-ol (**13**) [54]*

Palmitic acid (**11d**) (20 mmol, 5.128 g) was dissolved in anhydrous THF (80 mL) under argon and the solution was cooled in an ice bath (0 ºC). While stirring in the ice bath, $LiAlH_4$ (2.4 M in THF, 80 mmol, 33.3 mL) was added and the reaction mixture was allowed to warm to room temperature over 1 hour. The reaction mixture was stirred for a further 24 hours under argon at room temperature, and then quenched by careful addition of NaOH (1 M in H_2O, 60 mL). The reaction mixture was extracted with diethyl ether (2×70 mL). The organic phase was dried over anhydrous Na_2SO_4, filtered, and the volatile components evaporated in vacuo. Yield: 3.957 g (16.3 mmol, 81 %) of a white solid. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.88 (*t*, *J*=6.9 Hz, 3H), 1.19 – 1.39 (*m*, 27H), 1.52 – 1.61 (*m*, 2H), 3.64 (*t*, *J*=6.6 Hz, 2H).

*Synthesis of palmitaldehyde (**14**) [55]*

To a solution of hexadecan-1-ol (**13**) (16.3 mmol, 3.951 g) in anhydrous CH_2Cl_2 (100 mL), pyridinium chlorochromate (PCC, 24.5 mmol, ω = 0.98, 5.389 g) was added at room temperature and the reaction mixture was stirred for 16 h at room temperature. The solution was filtered through a plaque of Celite®, washed with CH_2Cl_2 and the volatiles evaporated *in vacuo*. The residue was purified by column chromatography (Silica gel 60, petroleum ether/ethyl acetate = 10:1). The fractions containing the pure product **14** were combined and the volatile components were evaporated *in vacuo*. Yield: 2.940 g (12.23 mmol, 75 %) of a colorless oil. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.88 (*t*, *J*=6.9 Hz, 3H), 1.26 (s, 24H), 1.58 – 1.67 (*m*, 2H), 2.42 (*td*, *J*=1.9, 7.4 Hz, 2H), 9.76 (*t*, *J*=1.9 Hz, 1H).

*Synthesis of 1-nitroheptadecan-2-ol (**15**)*

Prepared according to the literature procedure [56]. Palmitaldehyde (**14**) (11.44 mmol, 2.751 g) was dissolved in a mixture of anhydrous THF and anhydrous *t*-butanol in a 1:1 ratio (50 mL) under argon. Nitromethane (17.16 mmol, 930 µL) was then added at room temperature. The mixture was cooled to 0 °C, *t*BuOK (1.144 mmol, 128 mg) was added, and the reaction mixture was allowed to warm to room temperature over 1 hour. After 16 h at room temperature under argon, the reaction mixture was diluted with H_2O (300 mL) and the product was extracted with diethyl ether (2×100 mL). The organic phase was washed with NaCl (aq. sat., 2×50 mL), dried over anhydrous Na_2SO_4, filtered, and the volatiles evaporated *in vacuo*. The crude product **15** was used for the following transformation without further purification. Yield: 2.794 g (9.267 mmol, 81 %) of a yellowish oil. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.88 (*t*, *J*=6.9 Hz, 3H), 1.18 – 1.42 (*m*, 26H), 1.44 – 1.57 (*m*, 2H), 2.61 (br *s*, 1H), 4.28 – 4.34 (*m*, 1H), 4.38 (*dd*, *J*=8.5, 13.0 Hz, 1H), 4.43 (*dd*, *J*=2.7, 13.0 Hz, 1H).

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Synthesis of (E)*-1-nitroheptadec-1-ene (**16**) [66]*

Prepared according to the literature procedure [56]. 1-Nitroheptadecan-2-ol (**15**) (9.12 mmol, 2.75 g) was dissolved in anhydrous CH_2Cl_2 (25 mL) and cooled to –10 °C. With stirring, trifluoroacetic anhydride (TFAA, 9.12 mmol, 1.269 mL) was added dropwise and the cooled mixture (–10 °C) was stirred for another 2 minutes. Over the next 10 minutes, triethylamine (2.532 mL, 18.24 mmol) was added dropwise and the reaction mixture was stirred at –10 °C for another 30 minutes. The reaction mixture was then diluted with CH_2Cl_2 (100 mL) and washed with $NaHSO_4$ (aq., 1 M, 200 mL). The aqueous phase was extracted with CH_2Cl_2 (2×40 mL). The combined organic phase was dried over anhydrous Na_2SO_4, filtered, and the volatiles evaporated *in vacuo*. The residue was purified by column chromatography (Silica gel 60; petroleum ether/EtOAc = 40:1). The fractions containing the pure product **16** were combined and the volatile components were evaporated *in vacuo*. Product **16** was stored under argon at 5 °C. Yield: 2.016 g (7.114 mmol, 78 %) of a white solid; m.p. = 25.0–25.7 °C. EI-HRMS: *m*/*z* = 306.2395 (MNa^+); $C_{17}H_{34}NNaO_2$ requires: *m*/*z* = 306.2404 (MNa^+); ν_{max} 2922, 2853, 1650, 1526, 1465, 1350, 960, 835, 723 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.88 (*t*, *J*=6.9 Hz, 3H), 1.19 – 1.37 (*m*, 24H), 1.51 (*p*, *J*=7.3 Hz, 2H), 2.27 (*qd*, *J*=1.5, 7.4 Hz, 2H), 6.98 (*dt*, *J*=1.6, 13.4 Hz, 1H), 7.23 – 7.33 (*m*, 1H). ^{13}C-NMR (126 MHz, $CDCl_3$): δ 14.27, 22.84, 27.86, 28.61, 29.24, 29.40, 29.51, 29.59, 29.72, 29.77, 29.80, 29.82, 29.84, 32.07, 139.69, 143.01 (1 signal missing due to overlapping).

Organocatalyzed Michael addition of β-keto esters **2** *to nitroalkenes – General procedure for the preparation of racemic products* **rac-17** *– General procedure 3 (GP3)*

To a solution/suspension of nitroalkene **12** or **16** (0.2 mmol, 1.0 equivalent or 0.3 mmol, 1.5 equivalents) and the achiral organocatalyst **X** (0.04 mmol, 0.2 equivalents, 16.4 mg) in anhydrous CH_2Cl_2 (1 mL) under argon at room temperature, β-keto ester **2** (0.3 mmol, 1.5 equivalents or 0.2 mmol, 1.0 equivalent) was added and the resulting reaction mixture was stirred at room temperature for 24–72 hours. The volatiles were evaporated *in vacuo* and the residue was purified by column chromatography (Silica gel 60, mobile phase). The fractions containing the pure racemic product ***rac*-17** were combined and the volatiles were evaporated *in vacuo*. The product ***rac*-17** was fully characterized and analyzed by HPLC.

Organocatalyzed Michael addition of β-keto esters **2** *to nitroalkenes – General procedure for the organocatalyzed asymmetric addition – General procedure 4 (GP4)*

To a solution/suspension of nitroalkene **12** or **16** (0.2 mmol, 1.0 equivalent or 0.3 mmol, 1.5 equivalents) and the chiral organocatalyst **VIII** (0.02 mmol, 0.1 equivalents, 12.3 mg) or **I** (0.02 mmol, 0.1 equivalents, 10.9 mg) in anhydrous CH_2Cl_2 (1 mL) under argon at room temperature, β-keto ester **2** (0.3 mmol, 1.5 equivalents or 0.2 mmol, 1.0 equivalent) was added and the resulting reaction mixture was stirred at room temperature for 24–72 hours. The volatiles were evaporated *in vacuo* and the residue was purified by column chromatography (Silica gel 60, mobile phase). The fractions containing the pure chiral nonracemic product **17** were combined the volatiles were evaporated *in vacuo*. The product **17** was fully characterized and analyzed by HPLC.

*Synthesis of methyl 4-((*tert*-butoxycarbonyl)amino)-2-((*R*)-2-nitro-1-phenylethyl)-3-oxobutanoate (**17a**)*

Following *GP3* and *GP4*. Prepared from methyl 4-((*tert*-butoxycarbonyl)amino)-3-oxobutanoate (**2a**) (0.2 mmol, 46.3 mg) and *trans*-β-nitrostyrene (**12**) (0.3 mmol, 44.7 mg), organocatalyst **VIII**, 24 h; isolation by column chromatography (EtOAc/petroleum ether = 1:4). ***rac*-17a** Yield: 41.8 mg (0.110 mmol, 55%, two diastereomers in a ratio of 59:41 in DMSO-d_6) of white solid. **17a** Yield: 63.9 mg (0.168 mmol, 84%, two diastereomers in a ratio of 56:44 in DMSO-d_6) of white solid; m.p. = 116–122 °C. EI-HRMS: *m*/*z* = 381.1641 (MH^+); $C_{18}H_{25}N_2O_7$ requires: *m*/*z* = 381.1656 (MH^+); ν_{max} 3378, 2981, 1751, 1714, 1555, 1497, 1455, 1429, 1367, 1252, 1154, 1020, 974, 895, 858, 764, 699, 637 cm^{-1}. ^{1}H-NMR (500 MHz, DMSO-d_6) for major diastereomer: δ 1.39 (*s*, 9H), 3.37 (s, 3H), 3.95 (*dd*, *J*=3.5, 5.8 Hz, 2H), 4.06 – 4.13 (*m*, 1H), 4.40 (*d*, *J*=10.7 Hz, 1H), 4.87 – 4.96 (*m*, 2H), 7.18 (*t*, *J*=5.9 Hz, 1H), 7.22 – 7.34 (*m*, 5H). ^{1}H-NMR

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(500 MHz, DMSO-d_6) for minor diastereomer: δ 1.33 (*s*, 9H), 3.70 (*s*, 3H), 3.50 (*dd*, *J*=5.9, 18.8 Hz, 1H), 3.80 (*dd*, *J*=5.8, 18.8 Hz, 1H), 4.46 (*d*, *J*=10.2 Hz, 1H), 4.75 (*dd*, *J*=4.3, 13.2 Hz, 1H), 4.85 (*d*, *J*=10.8 Hz, 1H), 7.06 (*t*, *J*=5.8 Hz, 1H). ^{13}C-NMR (126 MHz, DMSO-d_6) for both diastereomers: δ 28.10, 28.14, 42.35, 42.65, 50.18, 50.25, 52.45, 52.84, 57.28, 57.93, 59.78, 77.74, 78.22, 78.24, 78.44, 127.79, 127.85, 128.18, 128.25, 128.49, 128.64, 136.85, 136.92, 155.47, 155.81, 167.33, 170.36, 199.88, 200.62 (3 signals missing due to overlapping). HPLC: Chiralpak IA-3, *n*-Hexane/*i*-PrOH = 80:20, flow rate 1.0 mL/min, λ = 210 nm, T = 20°C. Diastereomer 1: *t*R = 9.24 minutes (minor); 17.62 minutes (major) – 91% *ee*. Diastereomer 2: *t*R = 14.12 minutes (major); 23.56 minutes (minor) – 93% *ee*.

*Synthesis of methyl 5-((*tert*-butoxycarbonyl)amino)-2-((*R*)-2-nitro-1-phenylethyl)-3-oxopentanoate (**17b**) [22]*

Following *GP3* and *GP4*. Prepared from methyl 5-((*tert*-butoxycarbonyl)amino)-3-oxopentanoate (**2b**) (0.2 mmol, 49.1 mg) and *trans*-β-nitrostyrene (**12**) (0.3 mmol, 44.7 mg), organocatalyst **VIII**, 24 h; isolation by column chromatography (EtOAc/petroleum ether = 1:4). ***rac*-17b** Yield: 69.4 mg (0.176 mmol, 88%, two diastereomers in a ratio of 53:47 in DMSO-d_6) of white solid. **17b** Yield: 67.1 mg (0.170 mmol, 85%, two diastereomers in a ratio of 53:47 in DMSO-d_6) of white solid; m.p. = 96.1–98.4 °C. EI-HRMS: *m*/*z* = 417.1618 (MNa^+); $C_{19}H_{27}N_2NaO_7$ requires: *m*/*z* = 417.1632 (MNa^+); ν_{max} 3424, 2978, 1743, 1707, 1553, 1506, 1455, 1434, 1366, 1246, 1164, 1082, 966, 859, 756, 701 cm^{-1}. ^{1}H-NMR (500 MHz, DMSO-d_6) for both diastereomers: δ 1.34 (*s*, 4.5H), 1.37 (*s*, 4.5H), 2.24 – 2.34 (*m*, 0.5H), 2.58 – 2.68 (*m*, 0.5H), 2.74 (*t*, *J*=6.8 Hz, 1H), 2.76 – 2.91 (*m*, 1H), 3.15 (*q*, *J*=6.4 Hz, 1H), 3.35 (*s*, 1.5H), 3.70 (*s*, 1.5H), 4.00 – 4.09 (*m*, 1H), 4.37 (*dd*, *J*=6.0, 10.5 Hz, 1H), 4.81 (*d*, *J*=7.5 Hz, 1H), 4.87 – 4.99 (*m*, 1H), 6.58 (*t*, *J*=5.7 Hz, 0.5H), 6.85 (*t*, *J*=5.7 Hz, 0.5H), 7.21 – 7.35 (*m*, 5H). ^{13}C-NMR (126 MHz, DMSO-d_6) for both diastereomers: δ 28.19, 28.22, 34.52, 34.79, 42.30, 42.36, 42.66, 42.89, 52.43, 52.83, 60.00, 60.84, 77.69, 77.78, 78.00, 78.15, 127.79, 127.86, 128.27, 128.46, 128.63, 136.80, 136.96, 155.33, 155.53, 166.88, 167.72, 201.83 (6 signals missing due to overlapping). HPLC: Chiralpak IA-3, *n*-Hexane/*i*-PrOH = 80:20, flow rate 1.0 mL/min, λ = 210 nm, T = 20°C. Diastereomer 1: *t*R = 7.22 minutes (minor); 8.98 minutes (major) – 95% *ee*. Diastereomer 2: *t*R = 12.53 minutes (minor); 20.94 minutes (major) – 95% *ee*.

*Synthesis of methyl 2-(3-((*tert*-butoxycarbonyl)amino)propanoyl)-3-(nitromethyl)octadecanoate (**rac-17c**)*

Following *GP3*. Prepared from methyl 5-((*tert*-butoxycarbonyl)amino)-3-oxopentanoate (**2b**) (0.3 mmol, 73.6 mg) and (*E*)-1-nitroheptadec-1-ene (**16**) (0.2 mmol, 56.7 mg), organocatalyst **X**, 24 h; isolation by column chromatography (EtOAc/petroleum ether = 1:5). ***rac*-17c** Yield: 55.0 mg (0.104 mmol, 52%, two diastereomers in a ratio of 53:47 in $CDCl_3$) of colorless oil. EI-HRMS: *m*/*z* = 429.3313 (MH^+-Boc); $C_{23}H_{45}N_2O_5$ requires: *m*/*z* = 429.3323 (MH^+-Boc); ν_{max} 3413, 2923, 2853, 1743, 1712, 1552, 1505, 1436, 1366, 1248, 1168, 1084, 966, 911, 863, 781, 733 cm^{-1}. ^{1}H-NMR (600 MHz, $CDCl_3$) for the major diastereomer: δ 0.88 (*t*, *J*=6.9 Hz, 3H), 1.19 – 1.40 (*m*, 28H), 1.43 (*s*, 9H), 2.71 – 2.79 (*m*, 1H), 2.82 – 2.96 (*m*, 2H), 3.30 – 3.45 (*m*, 2H), 3.76 (*s*, 3H), 3.73 – 3.83 (*m*, 1H), 4.60 (*dd*, *J*=5.0, 12.9 Hz, 1H), 4.65 (*dd*, *J*=4.5, 13.2 Hz, 1H), 4.86 – 4.96 (*m*, 1H). ^{1}H-NMR (600 MHz, $CDCl_3$) for the minor diastereomer: δ 3.76 (*s*, 3H), 4.52 (*dd*, *J*=5.9, 13.1 Hz, 2H). ^{13}C-NMR (151 MHz, $CDCl_3$) for both diastereomers: δ 14.27, 22.83, 26.82, 26.88, 28.50, 29.42, 29.43, 29.49, 29.50, 29.63, 29.65, 29.74, 29.79, 29.81, 29.83, 29.84, 30.28, 32.06, 35.17, 36.64, 36.66, 43.35, 43.56, 52.94, 53.08, 59.31, 59.76, 76.02, 76.47, 79.58, 79.63, 155.95, 168.46, 203.83 (18 signals missing due to overlapping).

*Synthesis of methyl 4-((3-methylbut-2-en-1-yl)oxy)-2-((R)-2-nitro-1-phenylethyl)-3-oxobutanoate (**17d**)*

Following *GP3* and *GP4*. Prepared from methyl 4-((3-methylbut-2-en-1-yl)oxy)-3-oxobutanoate (**2c**) (0.2 mmol, 40.0 mg) and *trans*-β-nitrostyrene (**12**) (0.3 mmol, 44.7 mg), organocatalyst **VIII**, 24 h; isolation by column chromatography (EtOAc/petroleum ether = 1:5). ***rac*-17d** Yield: 54.5 mg (0.156 mmol, 78%, two diastereomers in a ratio of 60:40 in $CDCl_3$) of colorless oil. **17d** Yield: 62.2 mg (0.178 mmol, 89%, two diastereomers in a ratio of 60:40 in $CDCl_3$) of colorless oil. EI-HRMS: *m*/*z* = 367.1858 ($M+NH_4^+$); $C_{18}H_{27}N_2O_6$ requires: *m*/*z* = 367.1864 ($M+NH_4^+$); ν_{max} 3033, 2954, 2916, 1746, 1724, 1552, 1496,

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1434, 1378, 1247, 1199, 1169, 1092, 1034, 981, 942, 893, 766, 700, 618 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) for the major diastereomer: δ 1.61 (*s*, 3H), 1.74 (*s*, 3H), 3.73 (*s*, 3H), 3.76 – 3.90 (*m*, 2H), 4.21 – 4.32 (*m*, 3H), 4.79 – 4.95 (*m*, 3H), 5.20 – 5.24 (*m*, 1H), 7.18 – 7.24 (*m*, 2H), 7.25 – 7.33 (*m*, 3H). ^{1}H-NMR (500 MHz, $CDCl_3$) for the minor diastereomer: δ 1.66 (*s*, 3H), 1.75 (*s*, 3H), 3.52 (s, 3H), 3.98 (*d*, *J*=7.0 Hz, 2H), 4.02 (*d*, *J*=17.5 Hz, 1H), 4.10 (*d*, *J*=17.4 Hz, 1H). ^{13}C-NMR (126 MHz, $CDCl_3$): δ 18.12, 18.16, 25.90, 25.93, 42.13, 42.35, 52.80, 52.96, 56.60, 57.33, 67.75, 67.94, 74.72, 77.22, 77.77, 119.78, 119.80, 128.05, 128.22, 128.43, 128.50, 129.10, 129.22, 136.39, 136.41, 138.70, 138.84, 167.43, 167.90, 202.15, 202.77 (1 signal missing due to overlapping). HPLC: Chiralpak AS-H, *n*-Hexane/EtOH = 90:10, flow rate 1.0 mL/min, λ = 210 nm, T = 20 °C. Minor diastereomer: enantiomers: *t*R = 14.066 minutes (minor); 17.773 minutes (major) – 94% *ee*. Major diastereomer: enantiomers: *t*R = 17.164 minutes (major); 19.406 minutes (minor) – 91% *ee*.

*Synthesis of methyl 2-(2-((3-methylbut-2-en-1-yl)oxy)acetyl)-3-(nitromethyl)octadecanoate (**rac-17e**)*

Following *GP3*. Prepared from methyl 4-((3-methylbut-2-en-1-yl)oxy)-3-oxobutanoate (**2c**) (0.3 mmol, 60.1 mg) and (*E*)-1-nitroheptadec-1-ene (**16**) (0.2 mmol, 56.7 mg), organocatalyst **X**, 24 h; isolation by column chromatography (EtOAc/petroleum ether = 1:5). ***rac*-17e** Yield: 52.2 mg (0.108 mmol, 54%, two diastereomers in a ratio of 51:49 in $CDCl_3$) of colorless oil. EI-HRMS: *m*/*z* = 501.3887 ($M+NH_4^+$); $C_{27}H_{53}N_2O_6$ requires: *m*/*z* = 501.3898 ($M+NH_4^+$); ν_{max} 2923, 2853, 1726, 1553, 1435, 1379, 1250, 1199, 1158, 1092, 1000, 780, 722 cm^{-1}. ^{1}H-NMR (600 MHz, $CDCl_3$) for both diastereomers: δ 0.88 (*t*, *J*=7.0 Hz, 3H), 1.18 – 1.51 (*m*, 28H), 1.68 (*dd*, *J*=1.4, 4.8 Hz, 3H), 1.77 (*dd*, *J*=1.2, 4.1 Hz, 3H), 2.85 – 2.93 (*m*, 1H), 3.73 (*s*, 1.5H), 3.74 (*s*, 1.5H), 3.94 – 4.15 (*m*, 5H), 4.46 (*dd*, *J*=7.1, 13.3 Hz, 0.5H), 4.53 (*dd*, *J*=5.7, 13.2 Hz, 0.5H), 4.59 – 4.69 (*m*, 1H), 5.27 – 5.34 (*m*, 1H). ^{13}C-NMR (151 MHz, $CDCl_3$) for both diastereomers: δ 14.28, 18.19, 18.21, 22.84, 25.96, 26.88, 27.05, 29.38, 29.45, 29.51, 29.66, 29.75, 29.80, 29.83, 29.85, 30.29, 32.07, 36.10, 36.30, 52.67, 52.82, 54.92, 55.32, 67.99, 68.00, 74.63, 74.73, 76.40, 76.75, 119.82, 119.92, 138.71, 138.89, 168.55, 168.56, 203.55, 203.88 (17 signals missing due to overlapping).

*Synthesis of methyl 2-((R)-2-nitro-1-phenylethyl)-3-oxooctadecanoate (**17f**)*

Following *GP3* and *GP4*. Prepared from methyl 3-oxooctadecanoate (**2d**) (0.3 mmol, 93.7 mg) and *trans*-β-nitrostyrene (**12**) (0.2 mmol, 29.8 mg), organocatalyst **VIII**, 24 h; isolation by column chromatography (EtOAc/petroleum ether = 1:10). ***rac*-17f** Yield: 34.2 mg (0.074 mmol, 37%, two diastereomers in a ratio of 56:44 in $CDCl_3$) of white solid. **17f** Yield: 55.4 mg (0.120 mmol, 60%, two diastereomers in a ratio of 50:50 in $CDCl_3$) of white solid; m.p. = 60.0–61.2 °C. EI-HRMS: *m*/*z* = 462.3214 (MH^+); $C_{27}H_{44}NO_5$ requires: *m*/*z* = 462.3214 (MH^+); ν_{max} 2915, 2850, 1742, 1711, 1550, 1496, 1471, 1455, 1438, 1383, 1334, 1281, 1245, 1208, 1173, 1128, 1092, 1072, 1033, 1004, 983, 918, 892, 853, 765, 718, 700, 616 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) for the major diastereomer: δ 0.88 (*t*, *J*=6.9 Hz, 3H), 0.94 – 1.04 (*m*, 2H), 1.06 – 1.39 (*m*, 22H), 1.51 – 1.60 (*m*, 2H), 2.13 (*dt*, *J*=7.2, 17.8, 1H), 2.38 – 2.50 (*m*, 1H), 3.76 (*s*, 3H), 4.03 (*d*, *J*=10.0 Hz, 1H), 4.19 – 4.28 (*m*, 1H), 4.75 – 4.89 (*m*, 2H), 7.16 – 7.22 (*m*, 2H), 7.24 – 7.34 (*m*, 3H). ^{1}H-NMR (500 MHz, $CDCl_3$) for the minor diastereomer: δ 2.61 (*dt*, *J*=7.4, 17.7 Hz, 1H), 3.52 (*s*, 3H), 4.13 (*d*, *J*=9.5 Hz, 1H). ^{13}C-NMR (126 MHz, $CDCl_3$) for both diastereomers: δ 14.27, 22.83, 23.05, 23.39, 28.74, 29.00, 29.33, 29.45, 29.48, 29.50, 29.56, 29.68, 29.73, 29.76, 29.78, 29.80, 29.83, 32.06, 42.53, 42.86, 43.50, 43.84, 52.87, 53.05, 60.97, 61.34, 77.67, 77.93, 127.94, 128.11, 128.42, 128.50, 129.15, 129.26, 136.44, 136.63, 167.62, 168.14, 202.76, 203.81 (10 signals missing due to overlapping). HPLC: Chiralpak IA-3, *n*-Hexane/EtOH = 95:5, flow rate 1.0 mL/min, λ = 210 nm, T = 25 °C. Minor diastereomer: enantiomers: *t*R = 7.287 minutes (minor); 22.511 minutes (major) – 95% *ee*. Major diastereomer: enantiomers: *t*R = 8.963 minutes (major); 13.215 minutes (minor) – 96% *ee*.

*Synthesis of methyl 2-(1-nitroheptadecan-2-yl)-3-oxooctadecanoate (**rac-17g**)*

Following *GP3*. Prepared from methyl 3-oxooctadecanoate (**2d**) (0.3 mmol, 93.7 mg) and (*E*)-1-nitroheptadec-1-ene (**16**) (0.2 mmol, 56.7 mg), organocatalyst **X**, 24 h; isolation by column chromatography (EtOAc/petroleum ether = 1:10). ***rac*-17g** Yield: 78.7 mg (0.132 mmol, 66%, two

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diastereomers in a ratio of 68:32 in $CDCl_3$) of white solid; m.p. = 40.0–40.9 °C. EI-HRMS: *m/z* = 594.5108 ($M\text{-}H^+$)$^-$; $C_{36}H_{68}NO_5$ requires: *m/z* = 594.5103 ($M\text{-}H^+$)$^-$; ν_{max} 2955, 2914, 2849, 1730, 1707, 1556, 1543, 1470, 1435, 1402, 1380, 1243, 1204, 1128, 1073, 1000, 863, 719 cm^{-1}. ^{1}H-NMR (600 MHz, $CDCl_3$) for both diastereomers: δ 0.88 (*t*, *J*=7.0, 6H), 1.11 – 1.46 (*m*, 52H), 1.55 – 1.62 (*m*, 2H), 2.47 – 2.55 (*m*, 1H), 2.57 – 2.66 (*m*, 1H), 2.79 – 2.90 (*m*, 1H), 3.75 (*s*, 2.04H), 3.75 (*s*, 0.96H), 3.76 – 3.81 (*m*, 1H), 4.49 – 4.57 (*m*, 1H), 4.59 – 4.67 (m, 1H). ^{13}C-NMR (151 MHz, $CDCl_3$) for both diastereomers: δ 14.28, 22.85, 23.46, 23.50, 26.80, 26.91, 29.08, 29.10, 29.42, 29.45, 29.48, 29.50, 29.52, 29.60, 29.65, 29.67, 29.75, 29.81, 29.83, 29.85, 30.22, 32.08, 36.72, 36.77, 43.43, 43.60, 52.79, 52.91, 59.33, 59.72, 76.16, 76.57, 168.77, 168.81, 204.33, 204.46 (36 signals missing due to overlapping).

*Synthesis of methyl 2-((*R*)-2-nitro-1-phenylethyl)-3-oxoicosanoate (**17h**)*

Following *GP3* and *GP4*. Prepared from methyl 3-oxoicosanoate (**2e**) (0.3 mmol, 102.2 mg) and *trans*-β-nitrostyrene (**12**) (0.2 mmol, 29.8 mg), organocatalyst **VIII**, 24 h; isolation by column chromatography (EtOAc/petroleum ether = 1:10). ***rac*-17h** Yield: 43.1 mg (0.088 mmol, 44%, two diastereomers in a ratio of 54:46 in $CDCl_3$) of white solid. **17h** Yield: 52.9 mg (0.108 mmol, 54%, two diastereomers in a ratio of 48:52 in $CDCl_3$) of white solid; m.p. = 42.2–44.7 °C. EI-HRMS: *m/z* = 490.3524 (MH^+); $C_{29}H_{48}NO_5$ requires: *m/z* = 490.3527 (MH^+); ν_{max} 2914, 2849, 1737, 1712, 1555, 1496, 1471, 1455, 1433, 1404, 1378, 1271, 1198, 1168, 1113, 1082, 982, 891, 765, 716, 699 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) for the major diastereomer: δ 0.88 (*t*, *J*=6.9 Hz, 3H), 1.06 – 1.37 (*m*, 30H), 2.38 – 2.50 (*m*, 1H), 2.61 (*dt*, *J*=7.4, 17.7 Hz, 1H), 3.52 (*s*, 3H), 4.13 (*d*, *J*=9.4 Hz, 1H), 4.19 – 4.28 (*m*, 1H), 4.74 – 4.89 (*m*, 2H), 7.16 – 7.22 (*m*, 2H), 7.24 – 7.33 (*m*, 3H). ^{1}H-NMR (500 MHz, $CDCl_3$) for the minor diastereomer: δ 0.94 – 1.04 (*m*, 2H), 1.51 – 1.60 (*m*, 2H), 2.13 (*dt*, *J*=7.1, 17.7 Hz, 1H), 3.75 (*s*, 3H), 4.03 (*d*, *J*=10.0 Hz, 1H). ^{13}C-NMR (126 MHz, $CDCl_3$) for both diastereomers: δ 14.25, 22.82, 23.03, 23.37, 28.72, 28.99, 29.32, 29.43, 29.47, 29.49, 29.55, 29.67, 29.72, 29.75, 29.77, 29.79, 29.82, 32.05, 42.51, 42.86, 43.48, 43.83, 52.84, 53.02, 60.94, 61.33, 77.65, 77.92, 127.93, 128.10, 128.39, 128.47, 129.13, 129.24, 136.44, 136.63, 167.61, 168.12, 202.74, 203.79 (14 signals missing due to overlapping). HPLC: Chiralpak IA-3, *n*-Hexane/EtOH = 95:5, flow rate 1.0 mL/min, λ = 210 nm, T = 25 °C. Major diastereomer: enantiomers: *t*R = 8.838 minutes (minor); 26.885 minutes (major) – 96% *ee*. Minor diastereomer: enantiomers: *t*R = 10.913 minutes (major); 15.371 minutes (minor) – 96% *ee*.

*Synthesis of methyl 2-(1-nitroheptadecan-2-yl)-3-oxoicosanoate (**rac-17i**)*

Following *GP3*. Prepared from methyl 3-oxoicosanoate (**2e**) (0.3 mmol, 102.2 mg) and (*E*)-1-nitroheptadec-1-ene (**16**) (0.2 mmol, 56.7 mg), organocatalyst **X**, 24 h; isolation by column chromatography (EtOAc/petroleum ether = 1:10). ***rac*-17i** Yield: 52.4 mg (0.084 mmol, 42%, two diastereomers in a ratio of 50:50 in $CDCl_3$) of white solid; m.p. = 42.0–43.9 °C. EI-HRMS: *m/z* = 622.5416 ($M\text{-}H^+$)$^-$; $C_{38}H_{73}NO_5$ requires: *m/z* = 622.5421 ($M\text{-}H^+$)$^-$; ν_{max} 2956, 2915, 2848, 1731, 1706, 1556, 1542, 1470, 1435, 1402, 1379, 1349, 1241, 1205, 1128, 1108, 1078, 1001, 719 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) for both diastereomers: δ 0.87 (*t*, *J*=6.9 Hz, 6H), 1.08 – 1.44 (*m*, 56H), 1.53 – 1.61 (*m*, 2H), 2.45 – 2.55 (*m*, 1H), 2.56 – 2.66 (*m*, 1H), 2.78 – 2.89 (*m*, 1H), 3.74 (*s*, 1.5H), 3.74 (*s*, 1.5H), 3.75 (*d*, *J*=6.9 Hz, 0.5H), 3.79 (*d*, *J*=7.6 Hz, 0.5H), 4.45 – 4.55 (*m*, 1H), 4.62 (*td*, *J*=4.6, 13.5 Hz, 1H). ^{13}C-NMR (126 MHz, $CDCl_3$) for both diastereomers: δ 14.25, 22.83, 23.43, 23.48, 26.77, 26.88, 29.06, 29.08, 29.40, 29.43, 29.46, 29.48, 29.50, 29.59, 29.64, 29.71, 29.74, 29.79, 29.82, 29.84, 30.20, 32.06, 36.68, 36.74, 43.38, 43.56, 52.74, 52.86, 59.30, 59.69, 76.13, 76.54, 168.74, 168.78, 204.28, 204.41 (40 signals missing due to overlapping).

Synthesis of tert*-butyl 2-((*R*)-2-nitro-1-phenylethyl)-3-oxoicosanoate (**17j**)*

Following *GP3* and *GP4*. Prepared from *tert*-butyl 3-oxoicosanoate (**2f**) (0.3 mmol, 114.8 mg) and *trans*-β-nitrostyrene (**12**) (0.2 mmol, 29.8 mg), organocatalyst **VIII**, 24 h; isolation by column chromatography (EtOAc/petroleum ether = 1:10). ***rac*-17j** Yield: 42.5 mg (0.080 mmol, 40%, two diastereomers in a ratio of 61:39 in $CDCl_3$) of white solid. **17j** Yield: 50.0 mg (0.094 mmol, 47%, two diastereomers in a ratio of 36:64 in $CDCl_3$) of white solid; m.p. = 54.0–56.4 °C. EI-HRMS: *m/z* = 549.4273

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($M+NH_4^+$); $C_{32}H_{57}N_2O_5$ requires: m/z = 549.4262 ($M+NH_4^+$); ν_{max} 2916, 2849, 1731, 1712, 1553, 1496, 1468, 1434, 1394, 1378, 1284, 1250, 1148, 1126, 1092, 1062, 982, 914, 838, 770, 751, 720, 700 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) for the major diastereomer: δ 0.88 (*t*, *J*=6.9 Hz, 3H), 0.98 – 1.07 (*m*, 2H), 1.09 – 1.39 (*m*, 28H), 1.46 (*s*, 9H), 1.55 – 1.63 (*m*, 1H), 2.14 (*dt*, *J*=7.1, 17.5 Hz, 1H), 2.38 – 2.52 (*m*, 1H), 3.91 (*d*, *J*=9.9 Hz, 1H), 4.12 – 4.23 (*m*, 1H), 4.65 – 4.76 (*m*, 1H), 7.16 – 7.34 (*m*, 5H). ^{1}H-NMR (500 MHz, $CDCl_3$) for the minor diastereomer: δ 2.62 (*dt*, *J*=7.4, 17.4 Hz, 1H), 4.01 (*d*, *J*=10.1 Hz, 1H), 4.77 – 4.90 (*m*, 2H). ^{13}C-NMR (126 MHz, $CDCl_3$) for both diastereomers: δ 14.26, 22.83, 23.18, 23.53, 27.52, 27.98, 28.90, 29.15, 29.38, 29.48, 29.50, 29.56, 29.69, 29.73, 29.76, 29.80, 29.83, 32.06, 42.54, 42.79, 42.87, 43.59, 62.16, 62.51, 78.06, 78.40, 82.95, 83.40, 128.18, 128.29, 128.32, 128.36, 128.95, 129.14, 136.81, 136.84, 166.04, 166.75, 203.13, 203.98 (16 signals missing due to overlapping). HPLC: Chiralpak IA-3, *n*-Hexane/EtOH = 95:5, flow rate 1.0 mL/min, λ = 210 nm, T = 25 °C. Minor diastereomer: enantiomers: *t*R = 6.051 minutes (minor); 8.241 minutes (major) – 93% *ee*. Major diastereomer: enantiomers: *t*R = 6.768 minutes (minor); 7.403 minutes (major) – 98% *ee*.

Synthesis of tert*-butyl 2-(1-nitroheptadecan-2-yl)-3-oxoicosanoate (**rac-17k**)*

Following *GP3*. Prepared from *tert*-butyl 3-oxoicosanoate (**2f**) (0.3 mmol, 114.8 mg) and (*E*)-1-nitroheptadec-1-ene (**16**) (0.2 mmol, 56.7 mg), organocatalyst **X**, 24 h; isolation by column chromatography (first CC: CH_2Cl_2/petroleum ether = 1:3; second CC: EtOAc/petroleum ether = 1:10). ***rac*-17k** Yield: 51.9 mg (0.079 mmol, 39%, two diastereomers in a ratio of 66:34 in $CDCl_3$) of white solid; m.p. = 41.2–45.0 °C. EI-HRMS: m/z = 664.5894 $(M-H^+)^-$; $C_{41}H_{78}NO_5$ requires: m/z = 664.5886 $(M-H^+)^-$; ν_{max} 2916, 2848, 1726, 1703, 1556, 1545, 1466, 1370, 1256, 1210, 1157, 1047, 845, 720, 618 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) for both diastereomers: δ 0.88 (*t*, *J*=7.0 Hz, 6H), 1.12 – 1.44 (*m*, 56H), 1.47 (*s*, 9H), 1.55 – 1.63 (*m*, 2H), 2.45 – 2.54 (*m*, 1H), 2.56 – 2.67 (*m*, 1H), 2.76 – 2.86 (*m*, 1H), 3.63 (*d*, *J*=6.9, 0.34H), 3.66 (*d*, *J*=7.5 Hz, 0.66H), 4.48 – 4.56 (*m*, 1H), 4.57 – 4.67 (*m*, 1H). ^{13}C-NMR (126 MHz, $CDCl_3$) for both diastereomers: δ 14.26, 22.84, 23.55, 23.60, 26.79, 26.88, 28.03, 28.07, 29.23, 29.49, 29.51, 29.54, 29.60, 29.67, 29.76, 29.81, 29.83, 29.85, 30.19, 32.08, 36.66, 36.77, 43.26, 43.47, 60.43, 60.98, 76.40, 76.77, 83.01, 83.07, 167.40, 167.43, 204.68, 204.83 (44 signals missing due to overlapping).

*Synthesis of methyl (11Z,14Z)-2-((*R*)-2-nitro-1-phenylethyl)-3-oxoicosa-11,14-dienoate (**17l**)*

Following *GP3* and *GP4*. Prepared from methyl (11*Z*,14*Z*)-3-oxoicosa-11,14-dienoate (**2g**) (0.3 mmol, 101.0 mg) and *trans*-β-nitrostyrene (**12**) (0.2 mmol, 29.8 mg), organocatalyst **VIII**, 24 h; isolation by column chromatography (EtOAc/petroleum ether = 1:20). ***rac*-17l** Yield: 58 mg (0.120 mmol, 60%, two diastereomers in a ratio of 52:48 in $CDCl_3$) of colorless oil. **17l** Yield: 60.2 mg (0.124 mmol, 62%, two diastereomers in a ratio of 51:49 in $CDCl_3$) of colorless oil. EI-HRMS: m/z = 508.3032 (MNa^+); $C_{29}H_{43}NO_5Na$ requires: m/z = 508.3032 (MNa^+); ν_{max} 3009, 2925, 2855, 1744, 1717, 1554, 1496, 1455, 1434, 1377, 1243, 1168, 981, 914, 765, 699 cm^{-1}. ^{1}H-NMR (600 MHz, $CDCl_3$) for both diastereomers: δ 0.89 (*td*, *J*=1.5, 7.0 Hz, 3H), 0.95 – 1.05 (*m*, 1H), 1.10 – 1.16 (*m*, 1H), 1.16 – 1.21 (*m*, 1H), 1.23 – 1.40 (*m*, 12H), 1.52 – 1.60 (*m*, 1H), 1.97 – 2.07 (*m*, 4H), 2.13 (*dt*, *J*=7.2, 17.8 Hz, 0.5H), 2.39 – 2.49 (*m*, 1H), 2.61 (*dt*, *J*=7.4, 17.7 Hz, 0.5H), 2.77 (*q*, *J*=6.5 Hz, 2H), 3.52 (*s*, 1.5H), 3.76 (*s*, 1.5H), 4.03 (*d*, *J*=10.0 Hz, 0.5H), 4.13 (*d*, *J*=9.4 Hz, 0.5H), 4.19 – 4.27 (*m*, 1H), 4.74 – 4.88 (*m*, 2H), 5.28 – 5.43 (*m*, 4H), 7.17 – 7.21 (*m*, 2H), 7.22 – 7.34 (*m*, 3H). ^{13}C-NMR (151 MHz, $CDCl_3$) for both diastereomers: δ 14.22, 22.71, 23.03, 23.37, 25.76, 27.30, 27.31, 27.34, 28.70, 28.97, 29.13, 29.20, 29.24, 29.36, 29.48, 29.67, 29.72, 31.66, 42.53, 42.87, 43.48, 43.83, 52.87, 53.05, 60.98, 61.35, 77.67, 77.93, 127.94, 128.00, 128.02, 128.12, 128.20, 128.23, 128.43, 128.51, 129.16, 129.26, 130.13, 130.38, 136.45, 136.64, 168.14, 202.70, 203.76 (9 signals missing due to overlapping). HPLC: Chiralpak IA-3, *n*-Hexane/EtOH = 95:5, flow rate 1.0 mL/min, λ = 210 nm, T = 25 °C. Minor diastereomer: enantiomers: *t*R = 7.439 minutes (minor); 19.360 minutes (major) – 96% *ee*. Major diastereomer: enantiomers: *t*R = 9.402 minutes (major); 12.992 minutes (minor) – 96% *ee*.

*Synthesis of methyl (4*S*)-7-((*tert*-butoxycarbonyl)amino)-2-(2-nitro-1-phenylethyl)-3-oxo-4-stearamidoheptanoate (**17m**)*

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Following *GP3*. Prepared from methyl (*S*)-7-((*tert*-butoxycarbonyl)amino)-3-oxo-4-stearamidoheptanoate (**2h**) (0.2 mmol, 111.0 mg) and *trans*-β-nitrostyrene (**12**) (0.3 mmol, 44.7 mg), organocatalyst **X**, 48 h; isolation by column chromatography (1. EtOAc/petroleum ether = 1:2; 1. EtOAc/petroleum ether = 1:1). **17m** Yield: 100.0 mg (0.142 mmol, 71%, 4 diastereomers in a ratio of 27:21:24:28 in $CDCl_3$) of white semisolid. EI-HRMS: *m/z* = 704.4827 (MH^+); $C_{39}H_{66}N_3O_8$ requires: *m/z* = 704.4844 (MH^+); ν_{max} 3375, 2920, 2851, 1739, 1720, 1687, 1648, 1551, 1518, 1455, 1436, 1365, 1247, 1214, 1168, 1089, 1005, 872, 764, 720, 701, 617 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) for 4 diastereomers: δ 0.88 (*t*, *J*=6.9, 3H), 1.05 – 1.39 (*m*, 29H), 1.42 – 1.45 (*m*, 9H), 1.46 – 1.68 (*m*, 4H), 1.71 – 1.86 (*m*, 1H), 2.02 – 2.28 (*m*, 2H), 2.77 – 3.22 (*m*, 2H), 3.48, 3.49, 3.74, 3.77 (4 × *s*, 3H), 4.22 – 4.96 (*m*, 6H), 5.83 – 6.68 (m, 1H), 7.18 – 7.35 (*m*, 5H). ^{13}C-NMR (126 MHz, $CDCl_3$) for 4 diastereomers: δ 14.24, 22.80, 25.55, 25.62, 25.67, 25.90, 26.01, 26.20, 26.30, 26.90, 26.95, 27.05, 27.20, 28.48, 28.49, 29.38, 29.40, 29.43, 29.45, 29.47, 29.60, 29.61, 29.63, 29.73, 29.75, 29.77, 29.81, 32.03, 36.04, 36.40, 36.44, 36.50, 39.56, 39.71, 39.75, 42.54, 42.63, 43.10, 43.25, 52.84, 53.02, 53.11, 53.36, 57.89, 58.13, 58.32, 58.44, 58.62, 58.97, 59.18, 77.27, 77.36, 77.58, 77.70, 79.48, 79.52, 79.67, 79.70, 128.09, 128.14, 128.27, 128.36, 128.42, 128.50, 129.04, 129.18, 129.21, 136.21, 136.27, 136.50, 136.55, 156.26, 156.41, 156.55, 156.59, 166.95, 167.15, 167.30, 167.66, 173.10, 173.47, 173.85, 174.11, 200.93, 201.85, 202.18, 202.94 (69 signals missing due to overlapping).

*Synthesis of methyl 2-((S)-5-((tert-butoxycarbonyl)amino)-2-stearamidopentanoyl)-3-(nitromethyl)octadecanoate (**17n**)*

Following *GP3* and *GP4*. Prepared from methyl (*S*)-7-((*tert*-butoxycarbonyl)amino)-3-oxo-4-stearamidoheptanoate (**2h**) (0.2 mmol, 111.0 mg) and (*E*)-1-nitroheptadec-1-ene (**16**) (0.3 mmol, 85.0 mg), organocatalyst **X**, 48 h; isolation by column chromatography (1. EtOAc/petroleum ether = 1:3; 1. EtOAc/petroleum ether = 1:2); **17n** Yield: 129.1 mg (0.154 mmol, 77%, 4 diastereomers in a ratio of 26:28:25:21 in $CDCl_3$) of white solid. Organocatalyst **VIII**, 48 h; isolation by column chromatography (1. EtOAc/petroleum ether = 1:3; 1. EtOAc/petroleum ether = 1:2); **17n** Yield: 147.5 mg (0.176 mmol, 88%, 4 diastereomers in a ratio of 45:11:8:36 in $CDCl_3$) of white solid. EI-HRMS: *m/z* = 838.6860 (MH^+); $C_{48}H_{92}N_3O_8$ requires: *m/z* = 838.6879 (MH^+); ν_{max} 3361, 2917, 2850, 1741, 1718, 1687, 1644, 1553, 1524, 1467, 1366, 1250, 1222, 1171, 1039, 1011, 869, 721, 646 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) for 4 diastereomers: δ 0.88 (*t*, *J*=6.9 Hz, 6H), 1.10 – 1.39 (*m*, 57H), 1.44 (*s*, 9H), 1.48 – 1.58 (*m*, 2H), 1.58 – 1.67 (*m*, 2H), 1.87 – 1.99 (*m*, 1H), 2.20 – 2.27 (*m*, 2H), 2.80 – 2.93 (*m*, 1H), 3.05 – 3.24 (*m*, 2H), 3.73, 3.74, 3.76, 3.77 (4 × *s*, 3H), 3.99 (*d*, *J*=6.3 Hz, 0.206H), 4.04 (*d*, *J*=6.9 Hz, 0.255H), 4.09 (*d*, *J*=5.2 Hz, 0.284H), 4.15 (*d*, *J*=7.0 Hz, 0.255H), 4.40 – 4.80 (*m*, 4H), 6.42 – 6.58 (m, 1H). ^{13}C-NMR (126 MHz, $CDCl_3$) for 4 diastereomers: δ 14.23, 22.80, 25.67, 25.70, 26.36, 26.74, 26.77, 26.83, 26.87, 27.08, 27.43, 28.48, 29.42, 29.44, 29.46, 29.48, 29.64, 29.66, 29.72, 29.73, 29.75, 29.78, 29.82, 30.43, 30.52, 32.04, 36.37, 36.43, 36.53, 36.60, 37.22, 37.42, 39.76, 39.79, 39.82, 39.83, 52.77, 52.92, 53.00, 53.15, 55.92, 56.15, 56.47, 58.05, 58.26, 58.39, 58.62, 76.25, 76.43, 76.48, 77.36, 79.56, 156.45, 168.14, 168.38, 168.43, 168.46, 173.58, 173.64, 173.71, 173.80, 203.24, 203.40, 203.67 (128 signals missing due to overlapping).

*Synthesis of methyl (4S)-2-(2-nitro-1-phenylethyl)-3-oxo-4,7-distearamidoheptanoate (**17o**)*

Following *GP3*. Prepared from methyl (*S*)-3-oxo-4,7-distearamidoheptanoate (**2i**) (0.2 mmol, 144.1 mg) and *trans*-β-nitrostyrene (**12**) (0.3 mmol, 44.7 mg), organocatalyst **X**, 48 h; isolation by column chromatography (first column chromatography: EtOAc/petroleum ether = 1:1; second column chromatography: CH_2Cl_2/MeOH = 75:1). **17o** Yield: 50.5 mg (0.058 mmol, 29%, 4 diastereomers in a ratio of 24:22:30:24 in $CDCl_3$) of light orange solid. EI-HRMS: *m/z* = 870.6936 (MH^+); $C_{52}H_{92}N_3O_7$ requires: *m/z* = 870.6930 (MH^+); ν_{max} 3292, 2916, 2848, 1745, 1720, 1638, 1552, 1462, 1434, 1377, 1274, 1240, 1221, 1205, 1168, 1114, 755, 719, 700 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) for 4 diastereomers: δ 0.88 (*t*, *J*=6.9 Hz, 6H), 0.99 – 1.42 (*m*, 56H), 1.42 – 1.68 (*m*, 6H), 1.69 – 1.86 (*m*, 1H), 2.05 – 2.29 (*m*, 4H), 2.91 – 3.35 (*m*, 3H), 3.47, 3.48, 3.74, 3.77 (4 × *s*, 3H), 4.22 – 4.65 (*m*, 3H), 4.72 – 4.95 (*m*, 2H), 5.57 – 5.85 (m, 1H), 6.14 (*d*, *J*=7.9 Hz, 0.244H), 6.56 (*d*, *J*=7.9 Hz, 0.296H), 6.85 (br *s*, 0.225H), 6.93 (*d*, *J*=7.1 Hz, 0.235H), 7.18 – 7.34 (*m*, 5H). ^{13}C-NMR (126 MHz, $CDCl_3$) for 4 diastereomers: δ 14.24, 22.81, 25.55, 25.60, 25.63, 25.67, 25.77, 25.91, 26.08, 26.27, 26.57, 26.77, 27.03, 27.27, 29.41, 29.43, 29.48,

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29.50, 29.64, 29.66, 29.78, 29.80, 29.83, 32.04, 36.02, 36.38, 36.46, 36.89, 36.91, 38.52, 38.61, 38.68, 38.71, 42.54, 42.64, 43.09, 43.31, 52.83, 52.99, 53.14, 53.32, 58.08, 58.17, 58.19, 58.25, 58.27, 58.82, 58.95, 59.10, 77.29, 77.36, 77.56, 77.65, 77.69, 128.11, 128.16, 128.26, 128.36, 128.42, 128.49, 129.03, 129.17, 136.21, 136.33, 136.52, 136.60, 167.03, 167.21, 167.40, 167.69, 173.31, 173.74, 173.80, 174.07, 174.08, 174.21, 201.14, 201.89, 202.14, 203.10 (128 signals missing due to overlapping).

*Synthesis of methyl 2-((S)-2,5-distearamidopentanoyl)-3-(nitromethyl)octadecanoate (**17p**)*

Following *GP3* and *GP4*. Prepared from methyl (*S*)-3-oxo-4,7-distearamidoheptanoate (**2i**) (0.2 mmol, 144.1 mg) and (*E*)-1-nitroheptadec-1-ene (**16**) (0.3 mmol, 85.0 mg), organocatalyst **X**, 48 h; isolation by column chromatography (1. EtOAc/petroleum ether = 1:3; 1. EtOAc/petroleum ether = 1:1); **17p** Yield: 50.2 mg (0.05 mmol, 25%, 4 diastereomers in a ratio of 25:25:27:23 in $CDCl_3$) of light orange solid. Organocatalyst **VIII**, 48 h; isolation by column chromatography (1. EtOAc/petroleum ether = 1:3; 1. EtOAc/petroleum ether = 1:1); **17p** Yield: 46.2 mg (0.046 mmol, 23%, 4 diastereomers in a ratio of 39:11:12:38 in $CDCl_3$) of light orange solid. EI-HRMS: *m*/*z* = 1004.8949 (MH^+); $C_{61}H_{118}N_3O_7$ requires: *m*/*z* = 1004.8964 (MH^+); ν_{max} 3293, 2916, 2849, 1746, 1721, 1639, 1552, 1463, 1378, 1274, 1257, 1240, 1222, 1204, 719, 615 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) for 4 diastereomers: δ 0.88 (*t*, *J*=6.9, 9H), 1.07 – 1.46 (m, 88H), 1.48 – 1.70 (*m*, 7H), 1.83 – 1.98 (*m*, 1H), 2.14 – 2.21 (*m*, 2H), 2.21 – 2.30 (*m*, 2H), 2.81 – 2.92 (*m*, 1H), 3.17 – 3.28 (*m*, 1H), 3.28 – 3.40 (*m*, 1H), 3.73, 3.74, 3.76, 3.77 (4 × *s*, 3H), 3.98 (*d*, *J*=5.9 Hz, 0.235H), 4.03 (*d*, *J*=7.0 Hz, 0.270H), 4.08 (*d*, *J*=5.2 Hz, 0.249H), 4.14 (*d*, *J*=7.0 Hz, 0.246H), 4.37 – 4.78 (*m*, 3H), 5.79 – 5.89 (*m*, 1H), [6.72 (*d*, *J*=7.6 Hz), 6.76 (*d*, *J*=7.7 Hz), 6.77 (*d*, *J*=7.8 Hz), 6.89 (*d*, *J*=7.6 Hz); 1H]. ^{13}C-NMR (126 MHz, $CDCl_3$) for 4 diastereomers: δ 22.81, 25.65, 25.68, 25.69, 25.91, 25.93, 26.35, 26.41, 26.45, 26.49, 26.75, 26.79, 26.85, 26.89, 27.11, 27.40, 27.57, 29.44, 29.45, 29.49, 29.52, 29.57, 29.66, 29.67, 29.69, 29.71, 29.74, 29.76, 29.79, 29.81, 29.83, 30.44, 30.59, 32.05, 36.34, 36.39, 36.46, 36.48, 36.56, 36.92, 37.19, 37.40, 38.78, 38.81, 52.80, 52.94, 52.97, 53.16, 55.83, 55.89, 56.43, 56.55, 58.28, 58.41, 58.46, 58.56, 76.25, 76.50, 76.58, 77.36, 168.25, 168.36, 168.52, 173.80, 173.90, 173.94, 173.95, 174.02, 203.12, 203.63, 203.70 (173 signals missing due to overlapping).

*Organocatalyzed Michael addition of pyrrolones **11** to nitroalkene **16** – General procedure for the preparation of racemic mixtures – General procedure 5 (GP5)*

To a solution/suspension of (*E*)-1-nitroheptadec-1-ene (**16**) (0.2 mmol, 56.7 mg; 1.0 equivalent) and the achiral organocatalyst **X** (0.04 mmol, 0.2 equivalents, 16.4 mg) in anhydrous toluene (1 mL) under argon at room temperature, pyrrolone **11** (0.3 mmol, 1.5 equivalents) was added and the resulting reaction mixture was stirred at room temperature for 48–72 hours. The volatiles were evaporated *in vacuo* and the residue was purified by column chromatography (Silica gel 60, mobile phase). The fractions containing the pure racemic product ***rac*-18** were combined and the volatiles were evaporated *in vacuo*. The product ***rac*-18** was fully characterized and analyzed by HPLC.

*Organocatalyzed Michael addition of pyrrolones **11** to nitroalkene **16** – General procedure for the organocatalyzed asymmetric addition – General procedure 6 (GP6)*

To a solution/suspension of (*E*)-1-nitroheptadec-1-ene (**16**) (0.2 mmol, 56.7 mg; 1.0 equivalent) and the chiral organocatalyst **I** (0.02 mmol, 0.1 equivalents, 10.9 mg) in anhydrous toluene (1 mL) under argon at room temperature, pyrrolone **11** (0.3 mmol, 1.5 equivalents) was added and the resulting reaction mixture was stirred at room temperature for 48–72 hours. The volatiles were evaporated *in vacuo* and the residue was purified by column chromatography (Silica gel 60, mobile phase). The fractions containing the pure chiral nonracemic product **18** were combined the volatiles were evaporated *in vacuo*. The product **18** was fully characterized and analyzed by HPLC.

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*Synthesis of 1-(*tert*-butyl) 3-methyl (S)-5-benzyl-5-((S)-1-nitroheptadecan-2-yl)-4-oxo-4,5-dihydro-1H-pyrrole-1,3-dicarboxylate (**18a**)*

Following *GP5* and *GP6*. Prepared from 1-(*tert*-butyl) 3-methyl 5-benzyl-4-oxo-4,5-dihydro-1*H*-pyrrole-1,3-dicarboxylate (**11a**) (0.3 mmol, 99.4 mg) and (*E*)-1-nitroheptadec-1-ene (**16**) (0.2 mmol, 56.7 mg), organocatalyst **I**, 48 h; isolation by column chromatography (EtOAc/petroleum ether = 1:5). ***rac*-18a** Yield: 94.7 mg (0.154 mmol, 77%, diastereomer 1/diastereomer 2 = 97:3 in $CDCl_3$) of colorless oil. **18a** Yield: 84.8 mg (0.138 mmol, 69%, diastereomer 1/diastereomer 2 = 97:3 in $CDCl_3$) of colorless oil. EI-HRMS: *m*/*z* = 615.3970 (MH^+); $C_{35}H_{55}N_2O_7$ requires: *m*/*z* = 615.4004 (MH^+); ν_{max} 2923, 2853, 1732, 1713, 1581, 1554, 1497, 1456, 1438, 1370, 1295, 1224, 1143, 1089, 1063, 992, 914, 876, 843, 760, 725, 703, 628 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) for diastereomer 1: δ 0.88 (*t*, *J*=6.9 Hz, 3H), 1.07 – 1.43 (*m*, 26H), 1.44 – 1.85 (*m*, 11H), 3.26 – 3.54 (*m*, 3H), 3.77 (*s*, 3H), 4.31 (*dd*, *J*=5.1, 13.7 Hz, 1H), 4.51 (br *s*, 1H), 6.95 – 7.03 (*m*, 2H), 7.11 – 7.21 (*m*, 3H), 8.60 (br *s*, 1H). ^{1}H-NMR (500 MHz, $CDCl_3$) for diastereomer 2: δ 3.71 (*s*, 3H). ^{13}C-NMR (126 MHz, $CDCl_3$) for diastereomer 1: δ 14.26, 22.83, 27.55, 27.74, 28.10, 29.50, 29.52, 29.61, 29.63, 29.73, 29.78, 29.79, 29.82, 29.83, 32.06, 39.94, 43.20, 51.92, 76.56, 85.81, 112.39, 127.69, 128.43, 129.63, 133.25, 147.60, 161.78, 164.91, 196.43 (2 signals missing due to overlapping). HPLC: Chiralpak IA-3, *n*-Hexane/*i*PrOH = 95:5, flow rate 1.0 mL/min, λ = 210 nm, T = 25 °C. Major diastereomer: enantiomers: *t*R = 9.350 minutes (major); 13.217 minutes (minor) – 82% *ee*.

*Synthesis of 1-(*tert*-butyl) 3-methyl 5-(4-(((benzyloxy)carbonyl)amino)butyl)-5-(1-nitroheptadecan-2-yl)-4-oxo-4,5-dihydro-1H-pyrrole-1,3-dicarboxylate (**18b**)*

Following *GP5* and *GP6*. Prepared from 1-(*tert*-butyl) 3-methyl 5-(4-(((benzyloxy)carbonyl)amino)butyl)-4-oxo-4,5-dihydro-1*H*-pyrrole-1,3-dicarboxylate (**11b**) (0.3 mmol, 134.0 mg) and (*E*)-1-nitroheptadec-1-ene (**16**) (0.2 mmol, 56.7 mg), organocatalyst **I**, 72 h; isolation by column chromatography (EtOAc/petroleum ether = 1:2). ***rac*-18b** Yield: 94.9 mg (0.130 mmol, 65%, diastereomer 1/diastereomer 2 = 90:10 in $CDCl_3$) of colorless oil. **18b** Yield: 26.3 mg (0.036 mmol, 18%, diastereomer 1/diastereomer 2 = 26:74 in $CDCl_3$) of colorless oil. EI-HRMS: *m*/*z* = 730.4644 (MH^+); $C_{40}H_{64}N_3O_9$ requires: *m*/*z* = 730.4637 (MH^+); ν_{max} 3675, 3369, 2923, 2854, 1711, 1582, 1553, 1455, 1438, 1394, 1371, 1280, 1226, 1140, 1067, 846, 763, 697 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) for diastereomer 1: δ 0.88 (*t*, *J*=6.9 Hz, 3H), 0.91 – 1.03 (*m*, 2H), 1.06 – 1.34 (*m*, 27H), 1.35 – 1.49 (*m*, 4H), 1.56 (*s*, 9H), 1.96 – 2.07 (*m*, 1H), 2.10 – 2.22 (*m*, 1H), 3.03 – 3.17 (*m*, 3H), 3.84 (*s*, 3H), 4.22 (*dd*, *J*=5.3, 13.8 Hz, 1H), 4.30 – 4.41 (*m*, 1H), 4.71 (*t*, *J*=6.2 Hz, 1H), 5.06 (*s*, 2H), 7.27 – 7.39 (*m*, 5H). ^{1}H-NMR (500 MHz, $CDCl_3$) for diastereomer 2: δ 1.58 (*s*, 9H), 1.87 – 1.96 (*m*, 1H), 3.28 – 3.36 (*m*, 1H), 3.83 (*s*, 3H), 4.28 (*dd*, *J*=5.3, 14.6 Hz, 1H), 5.18 (*dd*, *J*=5.5, 14.7 Hz, 1H), 9.19 (*s*, 1H). ^{13}C-NMR (126 MHz, $CDCl_3$) for diastereomer 1: δ 14.26, 20.18, 22.82, 27.41, 27.49, 28.02, 29.49, 29.55, 29.62, 29.71, 29.77, 29.78, 29.81, 29.82, 32.05, 33.87, 40.61, 43.36, 52.03, 66.78, 76.35, 77.36, 86.22, 112.22, 128.24, 128.64, 136.59, 147.42, 156.40, 161.95, 165.24, 196.41 (4 signals missing due to overlapping). ^{13}C-NMR (126 MHz, $CDCl_3$) for diastereomer 1 and diastereomer 2 (diastereomer 1/diastereomer 2 = 26:74): δ 14.26, 20.19, 20.45, 22.82, 27.18, 27.50, 27.91, 28.03, 28.12, 29.44, 29.49, 29.50, 29.56, 29.63, 29.67, 29.72, 29.75, 29.79, 29.82, 29.83, 32.05, 33.89, 40.66, 41.98, 43.37, 52.03, 52.05, 66.79, 74.38, 76.11, 76.36, 77.40, 86.21, 112.23, 112.31, 128.25, 128.65, 136.59, 147.43, 156.39, 161.92, 165.29, 196.41, 197.67 (28 signals missing due to overlapping). HPLC: Chiralpak IA-3, *n*-Hexane/*i*PrOH = 90:10, flow rate 1.0 mL/min, λ = 210 nm, T = 25 °C. Major diastereomer: enantiomers: *t*R = 24.088 minutes (minor); 31.095 minutes (major) – 57% *ee*. Minor diastereomer: enantiomers: *t*R = 26.634 minutes (minor); 30.099 minutes (major) – 11% *ee*.

*Synthesis of 1-(*tert*-butyl) 3-methyl 5-(3-(benzyloxy)-3-oxopropyl)-5-(1-nitroheptadecan-2-yl)-4-oxo-4,5-dihydro-1H-pyrrole-1,3-dicarboxylate (**18c**)*

Following *GP5* and *GP6*. Prepared from 1-(*tert*-butyl) 3-methyl 5-(3-(benzyloxy)-3-oxopropyl)-4-oxo-4,5-dihydro-1*H*-pyrrole-1,3-dicarboxylate (**11c**) (0.3 mmol, 121.0 mg) and (*E*)-1-nitroheptadec-1-ene (**16**) (0.2 mmol, 56.7 mg), organocatalyst **I**, 48 h; isolation by column chromatography (EtOAc/petroleum ether = 1:5). ***rac*-18c** Yield: 92.0 mg (0.134 mmol, 67%, diastereomer 1/diastereomer

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2 = 93:7 in $CDCl_3$) of colorless oil. **18c** Yield: 42.6 mg (0.062 mmol, 31%, diastereomer 1/diastereomer 2 = 31:69 in $CDCl_3$) of colorless oil. EI-HRMS: *m*/*z* = 687.4224 (MH^+); $C_{38}H_{59}N_2O_9$ requires: *m*/*z* = 687.4215 (MH^+); ν_{max} 3675, 2923, 2854, 1735, 1713, 1582, 1554, 1439, 1393, 1371, 1279, 1256, 1227, 1141, 1077, 846, 800, 752, 698 cm^{-1}. ^{1}H-NMR (600 MHz, $CDCl_3$) for diastereomer 1: δ 0.88 (*t*, *J*=6.9 Hz, 3H), 1.17 – 1.34 (*m*, 27H), 1.35 – 1.46 (*m*, 1H), 1.56 (*s*, 9H), 1.98 – 2.06 (*m*, 1H), 2.09 – 2.17 (*m*, 1H), 2.37 – 2.45 (*m*, 1H), 2.48 – 2.55 (*m*, 1H), 3.13 – 3.20 (*m*, 1H), 3.83 (*s*, 3H), 4.25 (*dd*, *J*=5.6, 13.8 Hz, 1H), 4.30 – 4.39 (*m*, 1H), 5.07 (*s*, 2H), 7.28 – 7.39 (*m*, 5H), 9.08 (*s*, 1H). ^{1}H-NMR (500 MHz, $CDCl_3$) for diastereomer 2: δ 1.58 (*s*, 9H), 2.26 – 2.33 (*m*, 1H), 2.54 – 2.62 (*m*, 1H), 3.35 – 3.41 (*m*, 1H), 3.82 (*s*, 3H), 5.06 (*s*, 2H), 5.19 (*dd*, *J*=5.1, 14.7 Hz, 1H), 9.17 (*s*, 1H). ^{13}C-NMR (151 MHz, $CDCl_3$) for diastereomer 1: δ 14.26, 22.83, 27.48, 27.60, 28.01, 29.13, 29.49, 29.50, 29.54, 29.62, 29.72, 29.77, 29.79, 29.82, 29.84, 32.06, 43.15, 52.06, 66.88, 75.92, 76.42, 86.62, 112.16, 128.44, 128.47, 128.56, 128.75, 135.56, 147.29, 161.76, 165.19, 171.48, 195.61 (1 signal missing due to overlapping). ^{13}C-NMR (126 MHz, $CDCl_3$) for diastereomer 1 and diastereomer 2 (diastereomer 1/diastereomer 2 = 31:69): δ 14.28, 22.84, 27.17, 27.49, 28.02, 28.07, 28.11, 28.37, 29.28, 29.44, 29.50, 29.56, 29.64, 29.68, 29.73, 29.76, 29.80, 29.83, 29.85, 32.07, 41.85, 43.16, 52.06, 52.08, 66.89, 66.93, 74.46, 75.26, 75.93, 76.42, 77.39, 86.67, 112.15, 112.36, 128.45, 128.48, 128.58, 128.77, 135.51, 135.56, 147.29, 161.72, 161.77, 165.20, 165.34, 171.18, 171.49, 195.63, 196.88 (19 signal missing due to overlapping). HPLC: Chiralpak IA-3, *n*-Hexane/*i*PrOH = 90:10, flow rate 1.0 mL/min, λ = 280 nm, T = 25 °C. Major diastereomer: enantiomers: *t*R = 10.649 minutes (major); 12.074 minutes (minor) – 68% *ee*. Minor diastereomer: enantiomers: *t*R = 9.991 minutes (minor); 12.514 minutes (major) – 38% *ee*.

*Synthesis of 4-hydroxy-3-(1-nitroheptadecan-2-yl)furan-2(5*H*)-one (**20**)*

To a solution of (*E*)-1-nitroheptadec-1-ene (**16**) (0.2 mmol, 56.7 mg) and the achiral organocatalyst **X** (0.04 mmol, 0.2 equivalents, 16.4 mg) in anhydrous CH_2Cl_2 (1 mL) under argon at room temperature, tetronic acid (**19**) (0.3 mmol, 30.0 mg) was added and the resulting reaction mixture was stirred at room temperature for 72 hours. The volatiles were evaporated *in vacuo* and the residue was purified by column chromatography (Silica gel 60, EtOAc/petroleum ether = 1:1). The fractions containing the pure product **20** were combined and the volatiles were evaporated *in vacuo*. Yield: 33.8 mg (0.088 mmol, 44%) of white solid; m.p. = 86.8-88.2 °C. EI-HRMS: *m*/*z* = 384.2741 (MH^+); $C_{21}H_{38}NO_5$ requires: *m*/*z* = 384.2744 (MH^+); ν_{max} 2918, 2850, 1714, 1611, 1547, 1428, 1381, 1348, 1279, 1260, 1129, 1097, 1044, 971, 954, 780, 720, 682, 658 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.88 (*t*, *J*=6.9 Hz, 3H), 1.09 – 1.35 (*m*, 26H), 1.50 – 1.60 (*m*, 1H), 1.65 – 1.77 (*m*, 1H), 3.37 (*tt*, *J*=5.6, 9.6 Hz, 1H), 4.53 (*dd*, *J*=5.6, 12.4 Hz, 1H), 4.71 – 4.81 (*m*, 3H), 10.97 (br *s*, 1H). ^{13}C-NMR (126 MHz, $CDCl_3$): δ 14.27, 22.84, 27.28, 29.44, 29.51, 29.62, 29.76, 29.79, 29.81, 29.84, 29.86, 29.99, 32.07, 32.87, 68.14, 76.88, 99.10, 177.35, 177.91 (2 signals missing due to overlapping).

X-ray Crystallography. Single-crystal X-ray diffraction data was collected on Agilent Technologies SuperNova Dual diffractometer with an Atlas detector using monochromated Mo-K$_\alpha$ radiation (λ = 0.71073 Å) at 150 K. The data was processed using CrysAlis PRO [67]. Using Olex2.1.2. [68], the structure was solved by direct methods implemented in SHELXS [69] or SHELXT [70] and refined by a full-matrix least-squares procedure based on F^2 with SHELXT-2014/7 [71]. All nonhydrogen atoms were refined anisotropicallly. Hydrogen atoms were placed in geometrically calculated positions and were refined using a riding model. The drawing and the analysis of bond lengths, angles and intermolecular interactions were carried out using Mercury [72] and Platon [73]. Structural and other crystallographic details on data collection and refinement for compound **17a** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC Deposition Number 2513139. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).

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5. Conclusions

Glycine-, β-alanine-, lysine-, glycolic acid-, palmitic acid-, stearic acid-, and linoleic acid-derived β-keto esters **2a–i**, as well as phenylalanine-, ornithine-, and glutamic acid-derived pyrrolones **11a**–c and tetronic acid (**19**), were used as nucleophiles for the organocatalyzed addition to *trans*-β-nitrostyrene (**12**) and the palmitic acid-derived nitroalkene **16** electrophiles. All racemic products ***rac*-17a–l**, ***rac*-18a–c**, and **20** were prepared using the achiral organocatalyst **X**. For products with HPLC-separable stereomers, chiral nonracemic 1,4-adducts **17a**,**b**,**d**,**f**,**h**,**j**,**l** and **18a–c** were resynthesized using bifunctional noncovalent organocatalysts **I** and/or **VIII**. The doubly fatty acid-derived products ***rac*-17g,i,k** could not be separated on chiral HPLC columns. β-Keto ester adducts **17a**,**b**,**d**,**f**,**h**,**j**,**l** were prepared with high enantioselectivity (91–98% *ee*) but low diastereoselectivity (*dr* up to 36:64) due to the epimerizable C-2 stereocenter. The (1*S*,2*S*)-absolute configuration of the stereoisomer of adduct **17a** (prepared with organocatalyst **I**) was determined by single-crystal X-ray diffraction analysis. Based on this, we assigned the (1*R*)-absolute configuration to the major enantiomer of both diastereomers of products **17a**, **17b**, **17d**, **17f**, **17h**, **17j**, and **17l** prepared with organocatalyst **VIII**. Products **17m–p**, prepared from the addition of lysine-derived β-keto esters **2h** and **2i**, showed low diastereoselectivity with both achiral **X** and chiral organocatalyst **VIII**. In the pyrrolone series, the best diastereoselectivity (*dr* = 97:3) and enantioselectivity (82% *ee* for the major diastereomer) were obtained with phenylalanine-derived pyrrolone **11a**, yielding adduct **18a**. The (1'*S*,5*S*)-absolute configuration of the major diastereomer of product **18a** was assigned based on our previous results in the series of 1,4-adducts of pyrrolones to nitroalkene acceptors [22]. Despite certain drawbacks, such as low diastereoselectivity and challenges in separating stereomers on chiral HPLC columns, this study demonstrates the ease of assembling readily available amino acid and fatty acid building blocks under ambient conditions for the synthesis of interesting classes of products.

Supplementary Materials: The following supporting information can be downloaded: copies of ^{1}H- and ^{13}C-NMR spectra; HPLC data, X-ray diffraction data.

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Conflicts of Interest: The authors declare no conflict of interest.

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