

A Versatile Route to *syn*- and *anti*- α -Amino β -Hydroxy Esters from β -Keto Esters by Dynamic Kinetic Resolution with Ru-SYNPHOS[®] Catalyst

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A general and practical synthesis of both *syn*- and *anti*- α -amino β -hydroxy esters with high levels of selectivity by the use of Ru-SYNPHOS[®] catalysts is reported. The key transformations include asymmetric hydrogenations of α -*N*-substituted β -keto esters protected as α -amido or α -amino hydrochloride derivatives, respectively. The Ru^{II}-catalyzed hydro-

genation of α -amino β -keto ester hydrochlorides affords the corresponding *anti*- α -amino β -hydroxy esters with high diastereoselectivities (up to 99%) and enantioselectivities (up to 97%) through dynamic kinetic resolution (DKR).

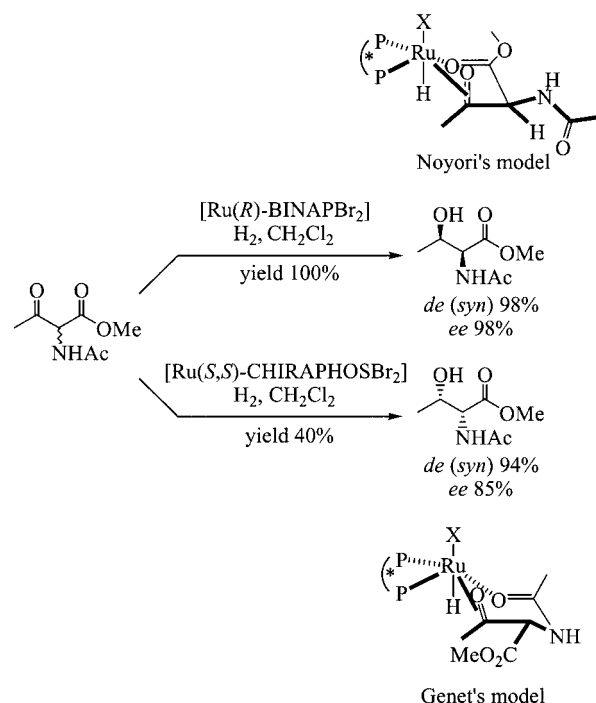
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Introduction

Amino acids and amino alcohols are finding increasing synthetic utility as intermediates for pharmaceutical and agricultural drugs.^[1,2] As representative examples, chiral α -amino β -hydroxy acids are important both as constituents of biologically active peptides^[3] and as key structural units in numerous bioactive natural products. D-*erythro*-Dihydro-sphingosine or D-*erythro*-sphingosine (inhibitor of protein kinase C) and their derivatives are involved in many biologically crucial processes from cell differentiation to signal transduction, while naturally occurring *anti*-(2*S*,3*S*)-3-hydroxyleucine is incorporated into the backbones of a range of peptide antibiotics and cyclopeptide alkaloids such as polyoxypeptins^[4] and papuamides.^[5] Chiral α -amino β -hydroxy acids are also components of glycopeptide antibiotics such as vancomycin.^[6] The synthesis of such compounds with high levels of selectivity remains a challenge, though many approaches have already been reported in the literature. An elegant and efficient pathway to *syn*- α -amino β -hydroxy esters through ruthenium-mediated hydrogenation of the corresponding α -amino β -keto esters by dynamic kinetic resolution (DKR) has been developed since the end of the 1980s. For access to the *anti* isomers, many different strategies such as sequential catalytic asymmetric hydrogenation and electrophilic amination have been described.^[7] Until very recently, however, there was no direct synthesis of these *anti* isomers by DKR.^[8]

DKR in association with Ru-catalyzed hydrogenation turned out to be a powerful synthetic tool to control two

adjacent stereogenic centers in one single chemical operation.^[9] It was originally reported simultaneously by Noyori^[10] and by our group^[11] in the context of the synthesis of threonine. The α -acetamido β -keto ester was efficiently hydrogenated, under optimized conditions, displaying high *syn* diastereoselectivity with (*R*)-BINAP- and (*S,S*)-CHIRAPHOS-ruthenium catalyst (Scheme 1). Since these pioneering works, this *syn* selection has been more generally obtained in the hydrogenation of acyclic α -amido



Scheme 1

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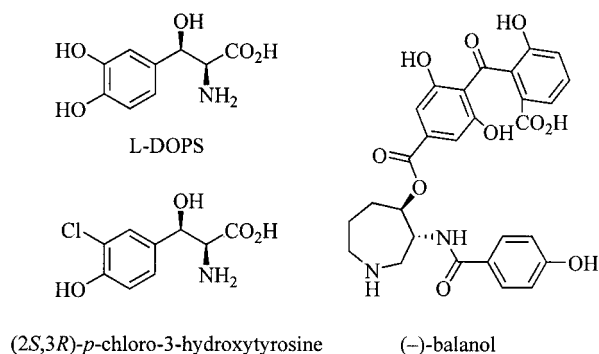


Figure 1. Representative examples of *syn* diastereoselectivity by DKR

β -keto esters. This efficient technology has been successfully applied to the total or formal synthesis of drugs (Figure 1) such as L-DOPS (an anti-Parkinsonian agent),^[10] biphenomycin A (an antibacterial agent),^[12] (-)-balanol (inhibitor of protein kinase C),^[13] and vancomycin-type β -hydroxytyrosine.^[14] This dynamic kinetic resolution^[10,15] has also been highlighted in the industrial synthesis of chiral 4-acetoxyazetidinone, followed by Ru^{III}-catalyzed oxidative acetoxylation,^[16] as precursor for β -carbapenem antibiotics.

Two different models to explain the origin of this *syn* diastereoselectivity have been suggested. Noyori's interpretation is based on a Felkin–Anh transition state, with reference to chelation of the ketone and the ester carbonyl function on the metal.^[9a,10] Another explanation has been proposed by our group, and is based on the formation of a transition chair-like chelate ruthenium amide complex in which the amide carbonyl group and the ketone are bonded to the metal (Scheme 1).^[11b]

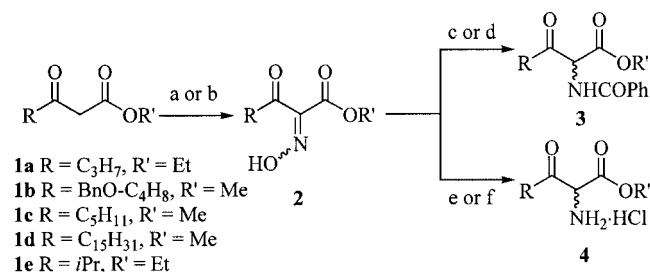
The selectivity of the dynamic kinetic resolution of α -substituted β -keto esters was then studied, and showed great dependence upon the reaction conditions and the nature of the configurationally labile group at the α position. The Ru-mediated hydrogenation of cyclic α -alkyl^[9a,10,17] or α -chloro β -keto esters^[18] gave the *anti* adducts. During preliminary work on Dolastatine 10, the *anti*- γ -amino β -hydroxy α -methyl ester, derived from (*S*)-proline, was isolated almost exclusively, as its amine hydrochloride salt, after asymmetric reduction of the corresponding β -keto α -methyl ester by DKR.^[19] On the basis of these previous studies and in our ongoing research into ruthenium-catalyzed asymmetric hydrogenation,^[20] we could reasonably hope that the outcome of the dynamic kinetic resolution of β -keto esters α -substituted with a $\text{NH}_2\cdot\text{HX}$ group ($\text{HX} = \text{HCl}$ or TsOH), displaying no chelating properties, would be in favor of the *anti* adducts.

The purpose of this communication is to report a straightforward synthesis of *anti*- α -amino β -hydroxy esters based on the dynamic kinetic resolution (DKR) of β -keto esters α -*N*-substituted as amine hydrochloride salts.

Results and Discussion

This study was conducted with a few examples of synthetic interest. Compounds **3** and **4** were easily prepared

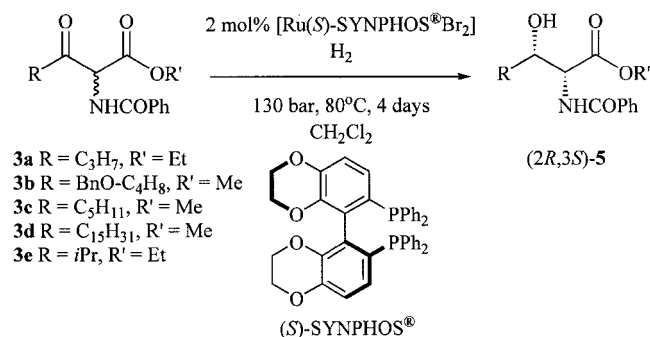
from the corresponding β -keto esters **1** in two steps according to the general scheme depicted below (Scheme 2).



Scheme 2. Reagents and conditions: (a) for **1a**, **1b**, **1e**, NaNO₂, AcOH/H₂O, > 84%; (b) for **1c**, **1d**, BuNO₂, HCl in Et₂O, Et₂O, > 91%; (c) for **1b** to **1e**, Zn, (PhCO)₂O, AcOH, 27 to 60%; (d) for **1a**, H₂, Pd/C, APTS, EtOH then PhCOCl, NEt₃, CH₂Cl₂, 81%; (e) for **1a**, **1c**, **1d**, **1e**, H₂, Pd/C, HCl in R'¹OH, quant.; (f) for **1b**, Zn, Boc₂O, AcOH then HCl in MeOH, MeOH, 82%.

The β -keto esters **1** were conveniently transformed into the oximes **2** by treatment with sodium nitrite in the presence of acetic acid or *n*-butyl nitrite in the presence of an ethereal solution of hydrochloric acid. These oximes **2** were reduced with zinc in acetic acid in the presence of benzoic anhydride to afford the desired α -benzamido β -keto esters **3**. This protecting group was preferred for its good chelating properties and for analytical facility (*de* and *ee* were determined by HPLC analysis). Our next concern was to prepare the requisite α -amino β -keto ester hydrochlorides **4**, starting from the same intermediates **2**. Compounds **4** were synthesized by using Pd/C and an alcoholic solution of hydrochloric acid under atmospheric pressure of hydrogen in quantitative yields. Because of the benzyloxy function in the substrate **1b** (R = BnO-C₄H₈), the corresponding α -amino β -keto ester hydrochloride **4b** was formed in a two-step procedure from **2b**, which was treated with zinc in the presence of Boc₂O, followed by addition of a methanolic solution of hydrochloric acid. The α -benzamido β -keto ester **3a** (R = C₃H₇) followed another synthetic pathway via the tosylate salt **6a**.

As expected, the *syn*- α -benzamido β -hydroxy esters **5** were synthesized in good yields (up to 92%) by hydrogenation of the corresponding β -keto esters **3** in dichloromethane. All the catalytic tests were performed with the chiral catalyst [Ru(diphosphane)Br₂] generated in situ, prepared from [(cod)(2-methylallyl)₂Ru], in the presence of the atropisomeric diphosphane ligand and methanolic HBr by our convenient procedure.^[21] Under optimized but drastic conditions, such as 130 bar of hydrogen at 80 °C for 4 days, with 2 mol % of Ru-SYNPHOS[®] [22] catalyst, good to excellent *syn* diastereoselectivities (86 to > 99% *de*) were observed. Except in the case of the substrate **3a** (R = C₃H₇, Entries 1 and 6, 75 and 86% *ee*, respectively), excellent levels of enantioselectivity were achieved (97–99% *ee*) (Scheme 3 and Table 1).



Scheme 3

Table 1. Hydrogenation of the α -benzamido β -keto esters **3**

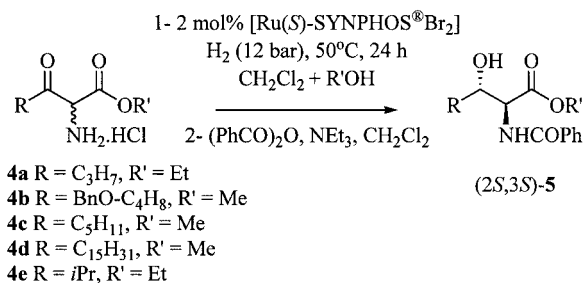
Entry ^[a]	Substrate	Yield [%]	<i>de</i> [%] ^[b]	<i>ee</i> [%] ^[b]
1	3a R = C ₃ H ₇	81	71	75 (2 <i>R</i> ,3 <i>S</i>)
2	3b R = BnO-C ₄ H ₈	53	93	> 99 (2 <i>R</i> ,3 <i>S</i>)
3	3c R = C ₅ H ₁₁	77	98	99 (2 <i>R</i> ,3 <i>S</i>)
4	3d R = C ₁₅ H ₃₁	82	98	97 (2 <i>R</i> ,3 <i>S</i>)
5	3e R = <i>i</i> Pr	92	99	97 (2 <i>R</i> ,3 <i>S</i>)
6 ^[c]	3a R = C ₃ H ₇	88	86	86 (2 <i>S</i> ,3 <i>R</i>)
7 ^[c]	3b R = BnO-C ₄ H ₈	70	92	> 99 (2 <i>S</i> ,3 <i>R</i>)
8 ^[c]	3c R = C ₅ H ₁₁	83	95	99 (2 <i>S</i> ,3 <i>R</i>)
9 ^[c]	3d R = C ₁₅ H ₃₁	92	98	97 (2 <i>S</i> ,3 <i>R</i>)
10 ^[c]	3e R = <i>i</i> Pr	94	> 99	98 (2 <i>S</i> ,3 <i>R</i>)

^[a] Conversion rates were determined by ¹H NMR (CDCl₃) spectroscopy; all reactions were complete. ^[b] *de* and *ee* were determined by HPLC analysis. ^[c] Reactions conducted with (*R*)-SYNPHOS® ligand.

It is noteworthy that the diastereoisomeric excesses obtained are directly linked to the steric hindrance created by the side chain; the higher the steric hindrance, the better the diastereoselectivity of the reaction [for the long chain **3d** (R = C₁₅H₃₁) or branched chain **3e** (R = *i*Pr) substrates (Entries 4, 9 and 5, 10)].

We next examined the hydrogenation of the α -amino β -keto ester hydrochlorides **4** in alcoholic solvents such as methanol or ethanol under 12 bar of hydrogen, for 24 h, at 50 °C with 1 mol % of catalyst under the hydrogenation conditions previously applied to the hydrogenation of the

β -keto α -methyl ester derived from (*S*)-proline as its amine hydrochloride salt.^[19] We were pleased to find that the reactions proceeded smoothly under these mild conditions with complete conversions and significant levels of *anti* diastereoselectivity (up to 98% *de*) but with disappointing *ees* (36 to 88% *ee*), whatever the pressure (12 to 100 bar) and/or the temperature (50 to 100 °C). The crude hydrogenated products were treated with benzoic anhydride and triethylamine to afford the corresponding α -benzamido β -hydroxy esters **5**. The configurations of these adducts were determined by comparison with the previously synthesized *syn*- α -benzamido β -hydroxy esters and authentic samples.^[23] According to these preliminary results, we found that dichloromethane was the most appropriate solvent to slow down the reaction rate and favor better discrimination by the Ru-catalyst. Because of the poor solubility of the α -amino β -keto ester hydrochlorides **4** in dichloromethane, the hydrogenations were carried out with 9% of alcoholic solvent (MeOH or EtOH), allowing better homogeneity of the reaction medium. After optimization of the conditions, we found that 2 mol % of catalyst were required to ensure complete conversion and that the atropisomeric ligand SYNPHOS®, recently developed in our group,^[22] provided high selectivities (Scheme 4).



Scheme 4

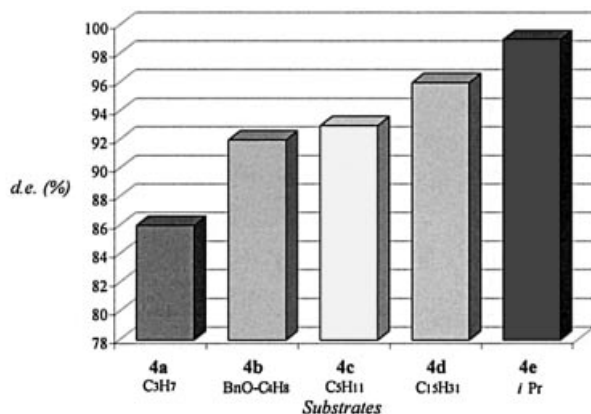
Both *anti*-(2*S*,3*S*) and (2*R*,3*R*) configurations of the α -benzamido β -hydroxy esters **5** were obtained efficiently with equal ease. The results are summarized in Table 2.

Table 2. Hydrogenation of the α -amino β -keto ester hydrochlorides **4** under optimized conditions

Entry ^[a]	Substrate	SYNPHOS® configuration	Yield [%] ^[b]	<i>de anti</i> [%] ^[c]	<i>ee</i> [%] ^[c]
1	4a R = C ₃ H ₇	(<i>S</i>)	90	86	92 (2 <i>S</i> ,3 <i>S</i>)
2		(<i>R</i>)	90	86	93 (2 <i>R</i> ,3 <i>R</i>)
3	4b R = BnO-C ₄ H ₈	(<i>S</i>)	94	92	92 (2 <i>S</i> ,3 <i>S</i>)
4		(<i>R</i>)	93	93	93 (2 <i>R</i> ,3 <i>R</i>)
5	4c R = C ₅ H ₁₁	(<i>S</i>)	85	93	91 (2 <i>S</i> ,3 <i>S</i>)
6		(<i>R</i>)	90	93	91 (2 <i>R</i> ,3 <i>R</i>)
7	4d R = C ₁₅ H ₃₁	(<i>S</i>)	83	96	96 (2 <i>S</i> ,3 <i>S</i>)
8		(<i>R</i>)	85	98	96 (2 <i>R</i> ,3 <i>R</i>)
9	4e R = <i>i</i> Pr	(<i>S</i>)	90	99	97 (2 <i>S</i> ,3 <i>S</i>)
10		(<i>R</i>)	96	97	96 (2 <i>R</i> ,3 <i>R</i>)

^[a] Reaction conditions: 0.5 mmol of substrate, S/C 50, 2 mL of CH₂Cl₂ and 200 μ L of R'OH (MeOH or EtOH), P(H₂):12 bar, 50 °C, 24 h. Conversion rates were determined by ¹H NMR (MeOD) spectroscopy before reprotection; all reactions were complete. ^[b] Yields over 2 steps. ^[c] *de* and *ee* were determined by HPLC analysis.

Finally, high enantioselectivities (from 91 to 97%) and diastereoselectivities, ranging from 86% for **4a** (R = C₃H₇, Entries 1 and 2) to 99% for **4e** (R = *i*Pr, Entry 9), were achieved with this catalytic system. Once again, the *de* followed the same tendency as previously observed, according to the nature of the side chain and its hindrance (Scheme 5).



Scheme 5. Influence of the side chain on the diastereoselectivity of the hydrogenation reaction (reaction conducted with Ru-(S)-SYNPHOS® catalyst)

Subsequent reaction optimization studies revealed that the hydrogenation reaction did not proceed completely under 6 bar of hydrogen even if the reaction time was increased to 36 h. Furthermore, the catalyst derived from [Ru(*p*-cymene)Cl₂]₂ (prepared simply in situ by mixing this ruthenium precursor with the atropisomeric diphosphane) was less effective in terms of yield. Another counter-anion was investigated for the C₃-substrate, which gave lower selectivities. With use of the tosylate derivative **6a** in the hydrogenation reaction under these optimized conditions, the reaction proceeded with *des* and *ees* decreasing from 86 to 80% and from 92 to 86%, respectively (Table 3). The hydrochloride salts seemed to be the most appropriate derivatives to achieve high selectivities.

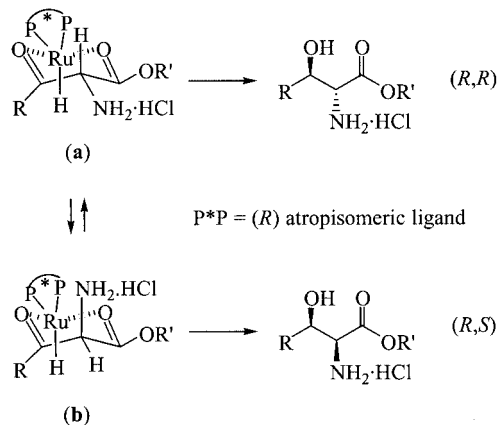
Table 3. Influence of the counter-anion on the selectivities

Entry	Substrate	SYNPHOS® configuration	<i>de, anti</i> [%] ^[b]	<i>ee</i> [%] ^[b]
1		(S)	86	92 (2 <i>S</i> ,3 <i>S</i>)
2		(R)	86	93 (2 <i>R</i> ,3 <i>R</i>)
3 ^[a]		(S)	79	86 (2 <i>S</i> ,3 <i>S</i>)
4 ^[a]		(R)	80	89 (2 <i>R</i> ,3 <i>R</i>)

^[a] TsOH = toluene-4-sulfonic acid. ^[b] *de* and *ee* were determined by HPLC analysis.

Although we have no clear evidence to explain the stereochemical outcome of the hydrogenation of these α -amino

β -keto ester hydrochlorides (high *anti* selectivity), we postulate that the reaction proceeds through a favored chair-like transition state (**a**) with the ketone and the ester carbonyl function chelated on the ruthenium and the NH₂·HCl group in an equatorial position rather than a transition state (**b**) with NH₂·HCl in an axial position (Scheme 6).



Scheme 6. Stereochemical model for *anti* stereoselectivity

Conclusion

Dynamic kinetic resolution of configurationally labile α -NH₂·HCl- β -keto esters with Ru-SYNPHOS® catalysts under mild conditions^[24] provides a direct and efficient route to *anti*- α -amino β -hydroxy esters with high levels of stereoselectivity. In this paper, we disclose an interesting alternative technology to our sequential approach by hydrogenation and electrophilic amination.^[7] Thanks to this convenient method, asymmetric hydrogenation emerges as an elegant and powerful tool for the synthesis of both *syn* and *anti* isomers of α -amino β -hydroxy acids, from the same common readily available intermediate 2-hydroxyimino β -keto ester. This study may confirm the role played by the chelating amide carbonyl function on the diastereoselectivity of the hydrogenation reaction of α -amido β -keto esters, as reported in our preliminary studies.^[11b] The scope of this reaction is still under investigation, and its application to the synthesis of natural products and their analogues is underway in our laboratory.

Experimental Section

General Remarks: Dichloromethane and dimethylformamide were distilled from calcium hydride, and diethyl ether from sodium-benzophenone. Acetone for the catalyst preparation was distilled from over potassium carbonate. Other solvents were used without any purification. Triethylamine was distilled from potassium hydroxide. All air- and/or water-sensitive reactions were carried out under an argon atmosphere unless otherwise noted. ¹H NMR spectra were recorded with an Avance 300 at 300 MHz or an Avance 400 at 400 MHz. ¹³C NMR spectra were recorded with an Avance 300 at 75 MHz or an Avance 400 at 100 MHz. Chemical shifts (δ) are reported in ppm downfield relative to internal Me₄Si. Coupling

constants (*J*) are reported in Hz and refer to apparent peak multiplicities (recorded as s, singlet; d, doublet; t, triplet; q, quadruplet; qu, quintet; o, octet; m, multiplet; and br., broad). Mass spectra were determined on a Nermag R10–10C instrument. Ionization was obtained by chemical ionization with ammonia (DCI/NH₃) or by electrospray (with a API 3000 PE Sciex instrument) for compounds **4** and **6a**. Optical rotations were measured with a Perkin–Elmer 241 polarimeter at 589 nm (sodium lamp). HPLC analyses of compounds **5** were conducted with Waters 600 system, using Daicel Chiralcel and Chiralpak chiral stationary phase columns. The β -keto esters **1a** and **1e** are commercially available.

Ethyl 2-Hydroxyimino-3-oxohexanoate (2a): A solution of ethyl 3-oxo-hexanoate (**1a**, 31 mmol, 4.91 g, 5 mL) in acetic acid (20 mL) was cooled to 0 °C, and a suspension of sodium nitrite (77.5 mmol, 2.5 equiv., 5.35 g) in water (17 mL) was added dropwise, the temperature of the reaction mixture being kept below 5 °C. After the evolution of brown fumes had ceased, the stirring was maintained at 0 °C for 2 h and at room temperature for 2.5 h. The reaction mixture was then diluted and extracted with diethyl ether (3 × 50 mL); the combined organic layers were washed with saturated aqueous sodium hydrogen carbonate, dried with magnesium sulfate and concentrated under reduced pressure to give the α -hydroxyimino β -keto ester **2a** quantitatively (5.75 g) as a clear oil. ¹H NMR (CDCl₃, 300 MHz): δ = 0.95 (t, *J* = 7.40 Hz, 3 H), 1.35 (t, *J* = 7.1 Hz, 3 H), 1.70 (m, 2 H), 2.76 (t, *J* = 7.3 Hz, 2 H), 4.38 (q, *J* = 7.1 Hz, 2 H), 9.15 (br. s, 1 H, OH) ppm. ¹³C NMR (CDCl₃, 75 MHz): δ = 13.6, 14.0, 17.1, 39.7, 62.3, 150.9, 161.4, 195.7 ppm. MS (DCI, NH₃): *m/z* (%) = 205 (100) [M + NH₄]⁺.

Methyl 7-Benzyloxy-2-hydroxyimino-3-oxoheptanoate (2b): A solution of methyl 7-benzyloxy-3-oxo-heptanoate (**1b**)^[25] (17 mmol, 4.50 g) in acetic acid (85 mL) was cooled to 0 °C and a suspension of sodium nitrite (42.5 mmol, 2.5 equiv., 2.90 g) in water (50 mL) was added dropwise, the temperature of the reaction mixture being kept below 5 °C. After the evolution of brown fumes had ceased, the stirring was maintained at 0 °C for 2 h. The reaction mixture was then diluted and extracted with diethyl ether (3 × 50 mL); the combined organic layers were washed with saturated aqueous sodium hydrogen carbonate, dried with magnesium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with cyclohexane/ethyl acetate (7:3) as eluent to give the desired product **2b** (4.18 g, 84% yield) as a white solid. M.p. 52 °C. ¹H NMR (CDCl₃, 300 MHz): δ = 1.72 (m, 4 H), 2.83 (t, *J* = 6.9 Hz, 2 H), 3.52 (t, *J* = 6.0 Hz, 2 H), 3.91 (s, 3 H), 4.54 (s, 2 H), 7.34 (m, 5 H), 9.65 (s, 1 H, OH) ppm. ¹³C NMR (CDCl₃, 75 MHz): δ = 20.3, 29.0, 37.4, 52.6, 70.0, 73.0, 127.9, 128.4, 137.4, 150.4, 162.2, 195.6 ppm. MS (DCI, NH₃): *m/z* (%) = 311 (100) [M + NH₄]⁺, 294 (3) [M + H]⁺.

Methyl 2-Hydroxyimino-3-oxooctanoate (2c): *n*-Butyl nitrite (23.22 mmol, 2 equiv., 2.63 mL) was added to a solution of methyl 3-oxooctanoate (**1c**)^[26] (11.61 mmol, 2.0 g) in diethyl ether (25 mL). The resulting mixture was cooled to 0 °C prior to the dropwise addition of an ethereal solution of hydrochloric acid (2.6 N, 46.44 mmol, 4 equiv., 18 mL). The stirring was maintained at 0 °C for 1 h and at room temperature for 0.5 h. Cold water (100 mL) was then poured into the reaction mixture. The aqueous layer was decanted and extracted twice with diethyl ether, and the combined organic layers were dried with magnesium sulfate and condensed under reduced pressure to give the α -hydroxyimino β -keto ester as a slightly brown oil. The residue was purified by silica gel column chromatography with cyclohexane/ethyl acetate (8:2) as eluent to give the desired product **2c** (2.13 g, 91% yield) as a slightly yellow oil. ¹H NMR (CDCl₃, 300 MHz): δ = 0.88 (t, *J* = 7.0 Hz, 3 H),

1.29 (m, 4 H), 1.63 (qu, *J* = 7.4 Hz, 2 H), 2.78 (t, *J* = 7.4 Hz, 2 H), 3.89 (s, 3 H), 10.17 (s, 1 H, OH) ppm. ¹³C NMR (CDCl₃, 75 MHz): δ = 13.5, 22.1, 23.2, 31.0, 37.4, 52.6, 150.4, 162.2, 196.6 ppm. MS (DCI, NH₃): *m/z* (%) = 219 (100) [M + NH₄]⁺, 202 (2) [M + H]⁺.

Methyl 2-Hydroxyimino-3-oxooctadecanoate (2d):^[27] *n*-Butyl nitrite (20 mmol, 2 equiv., 2.3 mL) was added to a solution of methyl 3-oxooctadecanoate (**1d**)^[27] (10 mmol, 3.12 g) in diethyl ether (40 mL). The resulting mixture was cooled to 0 °C prior to the dropwise addition of an ethereal solution of hydrochloric acid (4 N, 40 mmol, 4 equiv., 10 mL). The stirring was maintained at 0 °C for one hour and at room temperature for 3 h. Cold water (125 mL) was then poured into the reaction mixture. The aqueous layer was decanted and extracted twice with diethyl ether, and the combined organic layers were dried with magnesium sulfate and condensed under reduced pressure to give the α -hydroxyimino β -keto ester **2d** quantitatively as a slightly yellow powder, which was used without purification in the following reactions. M.p. 49 °C. ¹H NMR (CDCl₃, 300 MHz): δ = 0.87 (t, *J* = 6.8 Hz, 3 H), 1.26 (br. s, 24 H), 1.62 (m, 2 H), 2.78 (t, *J* = 7.4 Hz, 2 H), 3.90 (s, 3 H), 9.0 (br. s, 1 H, OH) ppm. ¹³C NMR (CDCl₃, 75 MHz): δ = 14.1, 23.6, 23.7, 29.1, 29.5, 31.9, 37.8, 52.8, 150.6, 162.0, 196.1 ppm. MS (DCI, NH₃): *m/z* (%) = 359 (100) [M + NH₄]⁺.

Ethyl 2-Hydroxyimino-4-methyl-3-oxopentanoate (2e): A solution of ethyl 4-methyl-3-oxo-pentanoate (**1e**, 28 mmol, 4.42 g) in acetic acid (20 mL) was cooled to 0 °C, and a suspension of sodium nitrite (70 mmol, 2.5 equiv., 4.82 g) in water (15 mL) was added dropwise, the temperature of the reaction mixture being kept below 5 °C. After the evolution of brown fumes had ceased, the stirring was maintained at 0 °C for 2 h and at room temperature for 3 h. The reaction mixture was then diluted and extracted with diethyl ether (3 × 50 mL); the combined organic layers were washed with saturated aqueous sodium hydrogen carbonate, dried with magnesium sulfate, and concentrated under reduced pressure to give the α -hydroxyimino β -keto ester **2e** (4.71 g, 90% yield) as a white syrup, which partially solidified. ¹H NMR (CDCl₃, 300 MHz): δ = 1.16 (d, *J* = 6.9 Hz, 6 H), 1.28 (t, *J* = 7.2 Hz, 3 H), 3.32 (hept, *J* = 6.9 Hz, 1 H), 4.30 (q, *J* = 7.2 Hz, 2 H) ppm. ¹³C NMR (CDCl₃, 75 MHz): δ = 13.9, 18.3, 35.5, 62.4, 149.7, 162.0, 201.1 ppm. MS (DCI, NH₃): *m/z* (%) = 205 (100) [M + NH₄]⁺.

Ethyl 2-Amino-3-oxohexanoate Tosylate Salt 6a: *p*-Toluenesulfonic acid (10 mmol, 1 equiv., 1.90 g) was added to a solution of ethyl 2-hydroxyimino-3-oxohexanoate (**2a**, 10 mmol, 1.87 g) in absolute ethanol (25 mL), followed by Pd/C 10% (3.33 mmol, 0.33 equiv., 355 mg). The argon was replaced with hydrogen, and the reaction mixture was stirred at room temperature under atmospheric pressure of hydrogen for 23 h. The suspension was then filtered through a celite pad and washed with absolute ethanol. The filtrate was concentrated under reduced pressure to give the tosylate salt **6a** as a white powder in quantitative yield. M.p. 95 °C. ¹H NMR (MeOD, 300 MHz): δ = 0.93 (t, *J* = 7.4 Hz, 3 H), 1.34 (t, *J* = 7.1 Hz, 3 H), 1.64 (sextuplet, *J* = 7.3 Hz, 3 H), 2.36 (s, 3 H), 2.72 (dt, *J* = 7.0, 25.1 Hz, 1 H), 2.86 (dt, *J* = 7.3, 18.1 Hz, 1 H), 4.35 (q, *J* = 7.1 Hz, 2 H), 7.22 (d, *J* = 8.0 Hz, 2 H), 7.70 (d, *J* = 8.0 Hz, 2 H) ppm. ¹³C NMR (MeOD, 100 MHz): δ = 13.7, 14.3, 17.7, 21.3, 43.3, 64.8, 127.0, 129.8, 141.7, 164.7, 199.6. ESI-MS: *m/z* = 196.3 [M – C₇H₈SO₃ + Na]⁺, 174.2 [M – C₇H₈SO₃ + H]⁺. HRMS (DCI⁺): *m/z* calcd. for C₈H₁₆NO₃: 174.1130; found 174.1128.

Ethyl 2-Benzoylamino-3-oxohexanoate (3a): Benzoyl chloride (4.5 mmol, 1.5 equiv., 522 μ L) was added to an ice-cooled solution of ethyl 2-amino-3-oxohexanoate tosylate salt **6a** (3 mmol, 1.03 g)

in dichloromethane (10 mL), followed by triethylamine (6 mmol, 2 equiv., 836 μ L). The stirring was maintained at 0 °C for 2 h before quenching with saturated aqueous ammonium chloride. The aqueous layer was decanted and extracted (3*) with dichloromethane. The combined organic layers were dried with magnesium sulfate and concentrated under reduced pressure to give a slightly yellow oil. The residue was purified by silica gel column chromatography with cyclohexane/ethyl acetate (9:1) as eluent to give **3a** (680 mg, 81% yield) as a white powder. M.p. 48 °C. ^1H NMR (CDCl_3 , 300 MHz): δ = 0.95 (t, J = 7.4 Hz, 3 H), 1.33 (t, J = 7.2 Hz, 3 H), 1.68 (sextuplet, J = 7.3 Hz, 2 H), 2.78 (m, 2 H), 4.30 (q, J = 7.2 Hz, 2 H), 5.41 (d, J = 6.4 Hz, 1 H), 7.30 (br. d, 1 H, *NH*), 7.48 (m, 3 H), 7.84 (m, 2 H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz): δ = 13.5, 14.0, 17.0, 42.7, 62.6, 62.9, 127.2, 128.6, 132.0, 133.1, 166.3, 166.8, 201.1 mS (DCI, NH_3): m/z (%) = 295 (28) $[\text{M} + \text{NH}_4]^+$, 278 (100) $[\text{M} + \text{H}]^+$. $\text{C}_{15}\text{H}_{19}\text{NO}_4$: calcd. C 64.97, H 6.91, N 5.05; found C 64.94, H 6.81, N 4.96.

General Procedure for the Synthesis of the α -Benzamido- β -keto Esters 3 (except for **3a):** Benzoic anhydride (2.2 equiv.) was added to a solution of 2-hydroxyimino β -keto ester **2** in acetic acid (2 mL/mmol), followed by zinc dust (7.7 equiv.) in small portions. The stirring was maintained at room temperature until completion of the reaction, as monitored by TLC. Water (10 mL/mmol) was then poured into the reaction mixture. The resulting mixture was filtered through a celite pad, and the zinc cake was washed with dichloromethane. The aqueous layer was decanted and extracted twice with dichloromethane. The combined organic layers were washed with saturated aqueous sodium hydrogen carbonate, dried with magnesium sulfate, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography.

Methyl 2-Benzoylamino-7-benzyloxy-3-oxoheptanoate (3b): This compound was obtained from **2b** (6 mmol, 1.76 g) by the General Procedure, by treatment with benzoic anhydride (13.2 mmol, 2.99 g) and zinc (46.2 mmol, 3.05 g), as a clear yellow oil (1.27 g, 54% yield); purification by silica gel column chromatography (cyclohexane/ethyl acetate, 8:2). ^1H NMR (CDCl_3 , 300 MHz): δ = 1.63 (m, 2 H), 1.74 (m, 2 H), 2.81 (m, 2 H), 3.46 (t, J = 6.1 Hz, 2 H), 3.78 (s, 3 H), 4.47 (s, 2 H), 5.44 (d, J = 6.5 Hz, 1 H), 7.29 (m, 5 H), 7.42 (t, J = 7.5 Hz, 2 H), 7.51 (t, J = 7.3 Hz, 1 H), 7.95 (d, J = 8.3 Hz, 2 H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz): δ = 20.2, 28.7, 40.4, 53.1, 62.6, 69.7, 72.7, 127.1, 127.4, 127.5, 128.2, 128.5, 131.9, 132.9, 138.3, 166.7, 200.8 ppm. MS (DCI, NH_3): m/z (%) = 401 (50) $[\text{M} + \text{NH}_4]^+$, 384 (100) $[\text{M} + \text{H}]^+$ ppm. HRMS (DCI $^+$): m/z calcd. for $\text{C}_{22}\text{H}_{26}\text{NO}_5$: 384.1811; found 384.1806.

Methyl 2-Benzoylamino-3-oxooctanoate (3c): This compound was obtained from **2c** (8.4 mmol, 1.69 g) by the General Procedure, by treatment with benzoic anhydride (18.5 mmol, 4.18 g) and zinc (64.7 mmol, 4.26 g), as a yellow oil (663 mg, 27% yield); purification by silica gel column chromatography (cyclohexane/ethyl acetate, 9:1). ^1H NMR (CDCl_3 , 300 MHz): δ = 0.88 (t, J = 6.9 Hz, 3 H), 1.30 (m, 4 H), 1.64 (qu, J = 7.2 Hz, 2 H), 2.76 (o, J = 7.2 Hz, 2 H), 3.81 (s, 3 H), 5.44 (d, J = 6.3 Hz, 1 H), 7.33 (br. d, J = 4.8 Hz, 1 H, *NH*), 7.44 (m, 2 H), 7.52 (t, J = 7.5 Hz, 1 H), 7.84 (d, J = 6.9 Hz, 2 H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz): δ = 13.8, 22.3, 23.3, 31.0, 40.8, 53.3, 62.8, 127.3, 128.6, 132.1, 132.9, 166.9, 201.2 ppm. MS (DCI, NH_3): m/z (%) = 309 (48) $[\text{M} + \text{NH}_4]^+$, 292 (100) $[\text{M} + \text{H}]^+$. $\text{C}_{16}\text{H}_{21}\text{NO}_4$: calcd. C 65.96, H 7.27, N 4.81; found C 66.04, H 7.24, N 4.76.

Methyl 2-Benzoylamino-3-oxooctadecanoate (3d): This compound was obtained from **2d** (6 mmol, 2.05 g) by the General Procedure, by treatment with benzoic anhydride (13.2 mmol, 2.99 g) and zinc

(46.2 mmol, 3.05 g), as a white powder (1.29 g, 50% yield); purification by silica gel column chromatography (cyclohexane/ethyl acetate, 8:2). M.p. 53 °C. ^1H NMR (CDCl_3 , 300 MHz): δ = 0.87 (t, J = 6.3 Hz, 3 H), 1.26 (br. s, 24 H), 1.52 (m, 2 H), 2.78 (dt, J = 3.4, 7.3 Hz, 2 H), 3.85 (s, 3 H), 5.44 (d, J = 6.5 Hz, 1 H), 7.32 (br. d, J = 6.5 Hz, 1 H, *NH*), 7.49 (m, 3 H), 7.84 (m, 2 H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz): δ = 14.1, 22.6, 23.4, 28.9, 29.4, 29.6, 31.9, 40.9, 53.3, 62.8, 127.3, 128.6, 132.1, 133.6, 166.8, 201.3 ppm. MS (DCI, NH_3): m/z (%) = 449 (27) $[\text{M} + \text{NH}_4]^+$, 432 (100) $[\text{M} + \text{H}]^+$ ppm. HRMS (DCI $^+$): m/z calcd. for $\text{C}_{26}\text{H}_{42}\text{NO}_4$: 432.3114; found 432.3109.

Ethyl 2-Benzoylamino-4-methyl-3-oxopentanoate (3e): This compound was obtained from **2e** (6 mmol, 1.12 g) by the General Procedure, by treatment with benzoic anhydride (13.2 mmol, 2.99 g) and zinc (46.2 mmol, 3.05 g), as a white powder (1.0 g, 60% yield); purification by silica gel column chromatography (cyclohexane/ethyl acetate, 8:2). M.p. 73 °C. ^1H NMR (CDCl_3 , 300 MHz): δ = 1.14 (d, J = 6.6 Hz, 3 H), 1.26 (d, J = 6.8 Hz, 3 H), 1.35 (t, J = 7.1 Hz, 3 H), 3.17 (heptuplet, J = 6.8 Hz, 1 H), 4.30 (q, J = 7.1 Hz, 2 H), 5.60 (d, J = 6.7 Hz, 1 H), 7.30 (br. d, 1 H, *NH*), 7.48 (m, 3 H), 7.84 (m, 2 H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz): δ = 14.0, 17.6, 18.9, 38.9, 61.2, 62.6, 127.2, 128.6, 132.0, 133.1, 166.4, 166.7, 205.2 ppm. MS (DCI, NH_3): m/z (%) = 295 (18) $[\text{M} + \text{NH}_4]^+$, 278 (100) $[\text{M} + \text{H}]^+$ ppm. HRMS (DCI $^+$): m/z calcd. for $\text{C}_{15}\text{H}_{20}\text{NO}_4$: 278.1392; found 278.1388.

General Procedure for the Synthesis of the α -Amino β -Keto Ester Hydrochlorides 4 (except for **4b):** Pd/C (10%, 0.33 equiv.) was added to a solution of 2-hydroxyimino β -keto ester **2** (5 mmol) in alcohol ($\text{R}'\text{OH}$) (3 mL/mmol). Alcoholic ($\text{R}'\text{OH}$) hydrochloric acid (3 N, 3 equiv.) was added dropwise to the resulting mixture, and the argon atmosphere was replaced with hydrogen. The reaction mixture was stirred at room temperature under atmospheric pressure of hydrogen for 24 h (reaction monitored by TLC). The suspension was then filtered through a celite pad and washed with $\text{R}'\text{OH}$. The filtrate was concentrated under reduced pressure to give the β -keto ester hydrochloride **4**.

Ethyl 2-Amino-3-oxohexanoate Hydrochloride (4a): This compound was obtained quantitatively from **2a** (5 mmol, 935 mg) by the General Procedure, by treatment with Pd/C (1.67 mmol, 178 mg) and ethanolic HCl (3 N, 15 mmol, 5 mL), as a slightly yellow powder. M.p. 121 °C. ^1H NMR (MeOD, 300 MHz): δ = 0.93 (t, J = 7.4 Hz, 3 H), 1.34 (t, J = 7.1 Hz, 3 H), 1.66 (sextuplet, J = 7.3 Hz, 2 H), 2.81 (qt, J = 7.1, 18.1 Hz, 2 H), 4.35 (q, J = 7.1 Hz, 2 H) ppm. ^{13}C NMR (MeOD, 75 MHz): δ = 13.3, 13.9, 17.3, 43.0, 64.4, 164.3, 199.1. ESI-MS: m/z = 196.3 $[\text{M} - \text{HCl} + \text{Na}]^+$, 174.4 $[\text{M} - \text{HCl} + \text{H}]^+$. HRMS (DCI $^+$): m/z calcd. for $\text{C}_8\text{H}_{16}\text{NO}_3$: 174.1130; found 174.1129.

Methyl 2-Amino-3-oxooctanoate Hydrochloride (4c): This compound was obtained quantitatively from **2c** (5 mmol, 1.0 g) by the General Procedure, by treatment with Pd/C (1.67 mmol, 178 mg) and methanolic HCl (3 N, 15 mmol, 5 mL), as a white powder. M.p. 76 °C. ^1H NMR (MeOD, 300 MHz): δ = 0.93 (t, J = 6.9 Hz, 3 H), 1.34 (m, 4 H), 1.65 (qu, J = 7.1 Hz, 2 H), 2.86 (qt, J = 7.1, 19.4 Hz, 2 H), 3.93 (s, 3 H) ppm. ^{13}C NMR (MeOD, 75 MHz): δ = 14.2, 23.4, 23.9, 32.1, 41.4, 54.6, 62.3, 165.3, 199.5. ESI-MS: m/z = 210 $[\text{M} - \text{HCl} + \text{Na}]^+$, 188 $[\text{M} - \text{HCl} + \text{H}]^+$. HRMS (DCI $^+$): m/z calcd. for $\text{C}_9\text{H}_{18}\text{NO}_3$: 188.1287; found 188.1289.

Methyl 2-Amino-3-oxooctadecanoate Hydrochloride (4d): This compound was obtained quantitatively from **2d** (4 mmol, 1.36 g) by the General Procedure, by treatment with Pd/C (1.33 mmol, 142 mg) and methanolic HCl (3 N, 12 mmol, 4 mL), as a slightly yellow

powder. dec. 200 °C. ^1H NMR (MeOD, 400 MHz): δ = 0.85 (d, J = 6.8 Hz, 3 H), 1.25 (s, 24 H), 1.59 (m, 2 H), 2.74 (dt, J = 6.8 Hz, 1 H), 2.85 (dt, J = 7.2 Hz, 1 H), 3.87 (s, 3 H) ppm. ^{13}C NMR (MeOD, 100 MHz): δ = 13.1, 22.3, 22.9, 28.6, 29.1, 29.2, 29.4, 31.7, 40.0, 53.2, 117.6, 163.9, 198.1. ESI-MS: m/z = 350.3 $[\text{M} - \text{HCl} + \text{Na}]^+$, 328.6 $[\text{M} - \text{HCl} + \text{H}]^+$. HRMS (DCI $^+$): m/z calcd. for $\text{C}_{19}\text{H}_{38}\text{NO}_3$: 328.2852; found 328.2862.

Ethyl 2-Amino-4-methyl-3-oxopentanoate Hydrochloride (4e): This compound was obtained quantitatively from **2e** (7 mmol, 1.31 g) by the General Procedure, by treatment with Pd/C (2.33 mmol, 248 mg) and ethanolic HCl (3 N, 21 mmol, 7 mL), as a slightly green powder. M.p. 115 °C. ^1H NMR (MeOD, 300 MHz): δ = 1.12 (d, J = 6.6 Hz, 3 H), 1.23 (d, J = 7.1 Hz, 3 H), 1.35 (t, J = 7.1 Hz, 3 H), 3.25 (q, J = 6.8 Hz, 1 H), 4.37 (q, J = 7.1 Hz, 2 H) ppm. ^{13}C NMR (MeOD, 100 MHz): δ = 14.2, 17.7, 19.1, 39.8, 64.8, 164.7, 203.8. ESI-MS: m/z = 369.3 $[2(\text{M} - \text{HCl}) + \text{Na}]^+$, 347.3 $[2(\text{M} - \text{HCl}) + \text{H}]^+$, 196.0 $[\text{M} - \text{HCl} + \text{Na}]^+$, 173.9 $[\text{M} - \text{HCl} + \text{H}]^+$. HRMS (DCI $^+$): m/z calcd. for $\text{C}_8\text{H}_{16}\text{NO}_3$: 174.1130; found 174.1134.

Methyl 2-Amino-7-benzyloxy-3-oxoheptanoate Hydrochloride (4b): *tert*-Butoxycarbonyl anhydride (87 mmol, 11.6 equiv., 20 mL) was added to an ice-cooled solution of 2-hydroxyimino β -keto ester **2b** (7.50 mmol, 2.20 g) in acetic acid (35 mL), followed by zinc dust (75 mmol, 10 equiv., 4.26 g) in small portions. The reaction mixture was then heated at 50 °C for 1 h. After it had cooled down, water (85 mL) was added, the resulting mixture was filtered through a celite pad, and the zinc cake was washed with dichloromethane. The aqueous layer was decanted and extracted twice with diethyl ether. The combined organic layers were washed with saturated aqueous sodium hydrogen carbonate, dried with magnesium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with cyclohexane/ethyl acetate (95:5 $\rightarrow$ 80:20) as eluent to give the desired product (2.49 g, 87% yield) as a colorless oil. ^1H NMR (CDCl_3 , 300 MHz): δ = 1.43 (s, 9 H), 1.64 (m, 4 H), 2.65 (m, 2 H), 3.45 (t, J = 6.0 Hz, 2 H), 3.76 (s, 3 H), 4.47 (s, 2 H), 5.02 (d, J = 7.1 Hz, 1 H), 5.73 (d, J = 7.1 Hz, 1 H, *NH*), 7.30 (m, 5 H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz): δ = 20.2, 28.2, 28.8, 40.2, 53.0, 63.4, 69.7, 72.8, 80.5, 127.5, 127.6, 128.3, 138.4, 154.8, 167.1, 201.1 ppm. MS (DCI, NH_3): m/z (%) = 397 (100) $[\text{M} + \text{NH}_4]^+$, 380 (13) $[\text{M} + \text{H}]^+$, 341 (35) $[\text{M} - \text{C}_4\text{H}_8 + \text{NH}_4]^+$. A solution of this α -NHBoc- β -keto ester (4 mmol, 1.50 g) in methanolic hydrochloric acid (3 N, 20 mmol, 5 equiv., 6.70 mL) was stirred at room temperature for 16 h. Methanolic hydrochloric acid (3 N, 20 mmol, 5 equiv., 6.70 mL) was added once more, and the stirring was maintained for an additional 6 h. Afterwards the solvent was removed under reduced pressure. The product **4b** was obtained as a white powder (1.19 g, 94% yield). M.p. 88 °C. ^1H NMR (MeOD, 300 MHz): δ = 1.68 (m, 4 H), 2.88 (m, 2 H), 3.51 (t, J = 6.0 Hz, 2 H), 3.89 (s, 3 H), 4.49 (s, 2 H), 7.30 (m, 5 H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz): δ = 21.2, 29.8, 41.1, 54.6, 71.0, 73.9, 128.7, 128.9, 129.4, 139.8, 165.2, 199.4. ESI-MS: m/z = 302.5 $[\text{M} - \text{HCl} + \text{Na}]^+$, 280.2 $[\text{M} - \text{HCl} + \text{H}]^+$. HRMS (DCI $^+$): m/z calcd. for $\text{C}_{15}\text{H}_{22}\text{NO}_4$: 280.1549; found 280.1552.

General Procedure for the in situ Preparation of the $[\text{Ru}(\text{SYNPHOS}^\text{®})\text{Br}_2]$ Catalyst: (*S*)- or (*R*)-SYNPHOS $^\text{®}$ (0.011 mmol, 1.1 equiv., 7.1 mg) and $\text{Ru}(\text{cyclooctadiene})[\eta^3\text{-(CH}_2)_2\text{CHCH}_3]_2$ (0.01 mmol, 3.2 mg) were placed in a 15 mL Schlenk tube and the vessel was purged with argon. Anhydrous acetone (1 mL), previously degassed by three vacuum-argon cycles, was added at room temperature. To this suspension was added, dropwise, methanolic hydrobromic acid (0.022 mmol, 2.2 equiv., 141 μL of a 0.156 N

solution prepared by addition of 48% aqueous HBr into degassed methanol) and the suspension was stirred at room temperature for 30 min. The suspension immediately turned yellow, and an orange precipitate then appeared. The solvent was thoroughly evaporated under vacuum to give the catalyst as an orange-brown solid, which was used directly.

General Procedure for the Synthesis of the *syn*- α -Amino β -Hydroxy Esters **5:** The α -benzamido β -keto ester **3** (0.5 mmol) was added to the catalyst $[\text{Ru}(\text{S})$ - or (*R*)-SYNPHOS $^\text{®}\text{Br}_2]$ (0.01 mmol, 2 mol %, prepared according to the General Procedure), followed by previously degassed anhydrous dichloromethane (2 mL). The Schlenk vessel was degassed by three vacuum-argon cycles and then placed under argon in a 250 mL stainless steel autoclave. The argon atmosphere was replaced with hydrogen by three cycles of pressurizing and the pressure was adjusted to 130 bar. The autoclave was heated at 80 °C and stirring was maintained for 4 days. After cooling, the reaction mixture was concentrated under reduced pressure to afford the crude α -benzamido β -hydroxy ester **5**. ^1H NMR spectroscopy showed a complete conversion.

Ethyl (2*R*,3*S*)-2-Benzoylamino-3-hydroxyhexanoate [(2*R*,3*S*)-5a**]:** This compound was obtained from **3a** (0.5 mmol, 139 mg) by the General Procedure, by treatment with $[\text{Ru}(\text{S})\text{-SYNPHOS}^\text{®}\text{Br}_2]$, as a yellow powder (113 mg, 81% yield); purification by silica gel column chromatography (cyclohexane/ethyl acetate, 7:3). Physical data identical to those of (2*S*,3*R*)-**5a**. $[\alpha]_\text{D}^{25} = -21$ (c = 1.0, CHCl_3). HPLC: Chiralcel OD-H, hexane/2-propanol (85:15), 0.5 mL/min, λ = 254 nm, t_R 11.84 min.

Ethyl (2*S*,3*R*)-2-Benzoylamino-3-hydroxyhexanoate [(2*S*,3*R*)-5a**]:** This compound was obtained from **3a** (0.5 mmol, 139 mg) by the General Procedure, by treatment with $[\text{Ru}(\text{R})\text{-SYNPHOS}^\text{®}\text{Br}_2]$, as a yellow powder (123 mg, 88% yield); purification by silica gel column chromatography (cyclohexane/ethyl acetate, 7:3). M.p. 70 °C. ^1H NMR (CDCl_3 , 300 MHz): δ = 0.92 (t, J = 7.0 Hz, 3 H), 1.31 (t, J = 7.2 Hz, 3 H), 1.40–1.56 (m, 4 H), 4.24 (m, 1 H, *CHOH*), 4.26 (m, 2 H), 4.85 (dd, J = 3.1, 7.0 Hz, 1 H, *CHNH*), 6.94 (br. d, J = 8.9 Hz, 1 H, *NH*), 7.45 (m, 3 H), 7.83 (m, 2 H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz): δ = 13.9, 14.1, 18.8, 36.0, 56.5, 61.7, 72.0, 127.2, 128.6, 131.8, 133.9, 167.8, 171.4 ppm. MS (DCI, NH_3): m/z (%) = 297 (19) $[\text{M} + \text{NH}_4]^+$, 280 (100) $[\text{M} + \text{H}]^+$. $\text{C}_{15}\text{H}_{21}\text{NO}_4$: calcd. C 64.50, H 7.58, N 5.01; found C 64.61, H 7.53, N 5.06. $[\alpha]_\text{D}^{25} = +21$ (c = 1.0, CHCl_3). HPLC: Chiralcel OD-H, hexane/2-propanol (85:15), 0.5 mL/min, λ = 254 nm, t_R 16.24 min.

Methyl (2*R*,3*S*)-2-Benzoylamino-7-benzyloxy-3-hydroxyheptanoate [(2*R*,3*S*)-5b**]:** This compound was obtained from **3b** (0.5 mmol, 191 mg) by the General Procedure, by treatment with $[\text{Ru}(\text{S})\text{-SYNPHOS}^\text{®}\text{Br}_2]$, as a slightly yellow oil (102 mg, 53% yield); purification by silica gel column chromatography (cyclohexane/ethyl acetate, 6:4). Physical data identical to (2*S*,3*R*)-**5b**. $[\alpha]_\text{D}^{25} = -18$ (c = 0.9, CHCl_3). HPLC: Chiralcel OD-H, 95:5 hexane/2-propanol, 1 mL/min, λ = 254 nm, t_R 37.59 min.

Methyl (2*S*,3*R*)-2-Benzoylamino-7-benzyloxy-3-hydroxyheptanoate [(2*S*,3*R*)-5b**]:** This compound was obtained from **3b** (0.5 mmol, 191 mg) by the General Procedure, by treatment with $[\text{Ru}(\text{R})\text{-SYNPHOS}^\text{®}\text{Br}_2]$, as a slightly yellow oil (135 mg, 70% yield); purification by silica gel column chromatography (cyclohexane/ethyl acetate, 6:4). ^1H NMR (CDCl_3 , 300 MHz): δ = 1.59 (m, 6 H), 3.02 (s, 1 H, *OH*), 3.48 (t, J = 6.0 Hz, 2 H), 3.77 (s, 3 H), 4.24 (m, 1 H, *CHOH*), 4.49 (s, 2 H), 4.88 (dd, J = 2.1, 9.0 Hz, 1 H, *CHNH*), 7.05 (d, J = 9.0 Hz, 1 H, *NH*), 7.28 (m, 5 H), 7.43 (t, J = 7.4 Hz, 2 H), 7.51 (t, J = 7.0 Hz, 1 H), 7.85 (d, J = 8.0 Hz, 2 H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz): δ = 22.4, 29.2, 33.5, 52.5, 56.6, 70.1, 71.9,

72.9, 127.2, 127.5, 127.6, 128.3, 128.5, 131.8, 133.7, 138.3, 167.8, 171.7 ppm. MS (DCI, NH₃): m/z (%) = 403 (4) [M + NH₄]⁺, 386 (100) [M + H]⁺ ppm. HRMS (DCI⁺): m/z calcd. for C₂₂H₂₈NO₅: 386.1967; found 386.1965. [α]_D²⁵ = +18 (c = 0.9, CHCl₃). HPLC: Chiralcel OD-H, hexane/2-propanol (95:5), 1 mL/min, λ = 254 nm, t_R 64.85 min.

Methyl (2*R*,3*S*)-2-Benzoylamino-3-hydroxyoctanoate [(2*R*,3*S*)-5c]: This compound was obtained from **3c** (0.5 mmol, 146 mg) by the General Procedure, by treatment with [Ru(*S*)-SYNPHOS®Br₂], as a slightly yellow oil (113 mg, 77% yield); purification by silica gel column chromatography (cyclohexane/ethyl acetate, 7:3). Physical data identical to those of (2*S*,3*R*)-**5c**. [α]_D²⁵ = −18 (c = 1.0, CHCl₃). HPLC: Chiralpak AS-H, hexane/2-propanol (98:2), 1.0 mL/min, λ = 254 nm, t_R 46.76 min.

Methyl (2*S*,3*R*)-2-Benzoylamino-3-hydroxyoctanoate [(2*S*,3*R*)-5c]: This compound was obtained from **3c** (0.5 mmol, 146 mg) by the General Procedure, by treatment with [Ru(*R*)-SYNPHOS®Br₂], as a slightly yellow oil (122 mg, 83% yield); purification by silica gel column chromatography (cyclohexane/ethyl acetate, 7:3). ¹H NMR (CDCl₃, 300 MHz): δ = 0.89 (t, J = 6.7 Hz, 3 H), 1.27–1.59 (m, 8 H), 3.77 (s, 3 H), 4.23 (m, 1 H, CHOH), 4.88 (dd, J = 2.0, 8.9 Hz, 1 H, CHNH), 7.04 (br. d, J = 8.9 Hz, 1 H, NH), 7.42 (t, J = 7.5 Hz, 1 H), 7.51 (t, J = 7.5 Hz, 1 H), 7.84 (d, J = 7.5 Hz, 2 H) ppm. ¹³C NMR (CDCl₃, 75 MHz): δ = 14.0, 22.5, 25.3, 31.5, 33.8, 52.6, 56.5, 72.1, 127.2, 128.6, 131.9, 133.7, 167.8, 171.9 ppm. MS (DCI, NH₃): m/z (%) = 311 (4%), [M + NH₄]⁺, 294 (100%), [M + H]⁺. C₁₆H₂₃NO₄: calcd. C 65.51, H 7.90, N 4.77; found C 65.50, H 7.95, N 4.68. [α]_D²⁵ = +16 (c = 1.0, CHCl₃). HPLC: Chiralpak AS-H, 98:2 hexane/2-propanol, 1.0 mL/min, λ = 254 nm, t_R 59.45 min.

Methyl (2*R*,3*S*)-2-Benzoylamino-3-hydroxyoctadecanoate [(2*R*,3*S*)-5d]: This compound was obtained from **3d** (0.5 mmol, 215 mg) by the General Procedure, by treatment with [Ru(*S*)-SYNPHOS®Br₂], as a white solid (178 mg, 82% yield); purification by silica gel column chromatography (cyclohexane/ethyl acetate 8:2). Physical data identical to those of (2*S*,3*R*)-**5d**. [α]_D²⁵ = −7 (c = 1.0, CHCl₃). HPLC: Chiralpak AS-H, 98:2 hexane/2-propanol, 1.0 mL/min, λ = 254 nm, t_R 24.13 min.

Methyl (2*S*,3*R*)-2-Benzoylamino-3-hydroxyoctadecanoate [(2*S*,3*R*)-5d]: This compound was obtained from **3d** (0.5 mmol, 215 mg) by the General Procedure, by treatment with [Ru(*R*)-SYNPHOS®Br₂], as a white solid (199 mg, 92% yield); purification by silica gel column chromatography (cyclohexane/ethyl acetate, 8:2). M.p. 72 °C. ¹H NMR (CDCl₃, 300 MHz): δ = 0.88 (t, J = 6.6 Hz, 3 H), 1.26 (br. s, 26 H), 1.50 (m, 2 H), 3.79 (s, 3 H), 4.24 (m, J = 2.0, 6.8 Hz, 1 H, CHOH), 4.88 (dd, J = 2.0, 8.9 Hz, 1 H, CHNH), 7.02 (br. d, J = 8.9 Hz, 1 H, NH), 7.48 (m, 3 H), 7.84 (m, 2 H) ppm. ¹³C NMR (CDCl₃, 75 MHz): δ = 14.1, 22.7, 25.7, 29.7, 31.9, 33.9, 52.6, 56.4, 72.1, 127.2, 128.6, 131.8, 133.8, 167.7, 171.9 ppm. MS (DCI, NH₃): m/z (%) = 434 (100) [M + H]⁺. C₂₆H₄₃NO₄: calcd. C 72.02, H 10.00, N 3.23; found C 72.03, H 10.03, N 3.28. [α]_D²⁵ = +6 (c = 1.0, CHCl₃). HPLC: Chiralpak AS-H, hexane/2-propanol (98:2), 1.0 mL/min, λ = 254 nm, t_R 29.59 min.

Ethyl (2*R*,3*S*)-2-Benzoylamino-3-hydroxy-4-methylpentanoate [(2*R*,3*S*)-5e]: This compound was obtained from **3e** (0.5 mmol, 139 mg) by the General Procedure, by treatment with [Ru(*S*)-SYNPHOS®Br₂], as a yellow oil (128 mg, 92% yield); purification by silica gel column chromatography (cyclohexane/ethyl acetate, 8:2). Physical data identical to those of (2*S*,3*R*)-**5e**. [α]_D²⁵ = −27 (c = 0.8, CHCl₃). HPLC: Chiralcel OJ, hexane/2-propanol (96:4), 1.0 mL/min, λ = 254 nm, t_R 17.57 min.

Ethyl (2*S*,3*R*)-2-Benzoylamino-3-hydroxy-4-methylpentanoate [(2*S*,3*R*)-5e]: This compound was obtained from **3e** (0.5 mmol, 139 mg) by the General Procedure, by treatment with [Ru(*R*)-SYNPHOS®Br₂], as a yellow oil (131 mg, 94% yield); purification by silica gel column chromatography (cyclohexane/ethyl acetate, 8:2). ¹H NMR (CDCl₃, 300 MHz): δ = 0.98 (d, J = 6.8 Hz, 3 H), 1.03 (d, J = 6.8 Hz, 3 H), 1.29 (t, J = 7.1 Hz, 3 H), 1.75 (m, 1 H), 3.82 (dd, J = 1.9, 8.9 Hz, 1 H, CHOH), 4.24 (q, J = 7.1 Hz, 2 H), 5.01 (dd, J = 1.9, 9.1 Hz, 1 H, CHNH), 6.91 (br. d, J = 9.1 Hz, 1 H, NH), 7.47 (m, 3 H), 7.83 (m, 2 H) ppm. ¹³C NMR (CDCl₃, 75 MHz): δ = 14.1, 18.9, 19.0, 31.1, 54.7, 61.7, 77.6, 127.2, 128.6, 131.8, 133.9, 167.8, 171.9 ppm. MS (DCI, NH₃): m/z (%) = 280 (100) [M + H]⁺. C₁₅H₂₁NO₄: calcd. C 64.50, H 7.58, N 5.01; found C 64.65, H 7.83, N 4.77. [α]_D²⁵ = +28 (c = 0.8, CHCl₃). HPLC: Chiralcel OJ, hexane/2-propanol (96:4), 1.0 mL/min, λ = 254 nm, t_R 13.25 min.

General Procedure for the Synthesis of the anti- α -Amino β -Hydroxy Esters 5: The α -amino β -keto ester hydrochloride **4** (0.5 mmol) was added to the catalyst [Ru(*S*)- or (*R*)-SYNPHOS®Br₂] (0.01 mmol, 2 mol%), prepared according to the general procedure), followed by previously degassed anhydrous dichloromethane (2 mL) and degassed alcoholic solvent R'OH (200 μ L). The Schlenk vessel was degassed by three vacuum-argon cycles and then placed under argon in a 250 mL stainless steel autoclave. The argon was replaced with hydrogen by three cycles of pressurizing and the pressure was adjusted to 12 bar. The autoclave was heated at 50 °C and stirring was maintained for 24 h. After cooling, the reaction mixture was concentrated under reduced pressure to afford the crude β -hydroxy ester. ¹H NMR (MeOD) spectroscopy showed complete conversion.

Benzoic anhydride (0.55 mmol, 1.1 equiv., 122 mg) was added to an ice-cooled solution of the crude α -amino β -hydroxy ester hydrochloride (0.5 mmol) in anhydrous dichloromethane (5 mL), followed by triethylamine (0.6 mmol, 1.2 equiv., 84 μ L). After the mixture had been kept for 15 min at 0 °C, the stirring was maintained at room temperature for 20 h. The mixture was then concentrated under reduced pressure. Tetrahydrofuran (10 mL) was added to the residue and the mixture was stirred for 15 minutes. The resulting precipitate was removed by filtration through a celite pad and washed with tetrahydrofuran. The filtrate was concentrated under reduced pressure and the crude product was purified by silica gel column chromatography.

Ethyl (2*S*,3*S*)-2-Benzoylamino-3-hydroxyhexanoate [(2*S*,3*S*)-5a]: This compound was obtained from **4a** (0.5 mmol, 105 mg) by the General Procedure, by treatment with [Ru(*S*)-SYNPHOS®Br₂], as a slightly yellow powder (125 mg, 90% yield over two steps); purification by silica gel column chromatography (cyclohexane/ethyl acetate, 7:3). M.p. 45 °C. ¹H NMR (CDCl₃, 300 MHz): δ = 0.92 (t, J = 7.0 Hz, 3 H), 1.31 (t, J = 7.2 Hz, 3 H), 1.26–1.56 (m, 4 H), 4.08 (m, 1 H, CHOH), 4.26 (m, 2 H), 4.85 (dd, J = 3.1, 7.0 Hz, 1 H, CHNH), 7.23 (br. d, J = 7.0 Hz, 1 H, NH), 7.45 (m, 3 H), 7.83 (m, 2 H) ppm. ¹³C NMR (CDCl₃, 75 MHz): δ = 13.9, 14.1, 18.9, 35.4, 58.2, 62.0, 73.0, 127.2, 128.6, 132.0, 133.4, 168.0, 170.5 ppm. MS (DCI, NH₃): m/z (%) = 297 (4) [M + NH₄]⁺, 280 (100), [M + H]⁺ ppm. HRMS (DCI⁺): m/z calcd. for C₁₅H₂₂NO₄: 280.1549; found 280.1552. [α]_D²⁵ = +32 (c = 1.0, CHCl₃). HPLC: Chiralcel OD-H, hexane/2-propanol (85:15), 0.5 mL/min, λ = 254 nm, t_R 14.99 min.

Ethyl (2*R*,3*R*)-2-Benzoylamino-3-hydroxyhexanoate [(2*R*,3*R*)-5a]: This compound was obtained from **4a** (0.5 mmol, 105 mg) by the General Procedure, by treatment with [Ru(*R*)-SYNPHOS®Br₂], as

a slightly yellow powder (125 mg, 90% yield over two steps); purification by silica gel column chromatography (cyclohexane/ethyl acetate, 7:3). Physical data identical to those of (2*S*,3*S*)-**5a**. $[\alpha]_D^{25} = -32$ ($c = 1.0$, CHCl_3). HPLC: Chiralcel OD-H, hexane/2-propanol (85:15), 0.5 mL/min, $\lambda = 254$ nm, t_R 12.59 min.

Methyl (2*S*,3*S*)-2-Benzoylamino-7-benzyloxy-3-hydroxyheptanoate [(2*S*,3*S*)-5b**]:** This compound was obtained from **4b** (0.5 mmol, 158 mg) by the General Procedure, by treatment with $[\text{Ru}(\text{S})\text{-SYNPHOS}^\text{®}\text{Br}_2]$, as a brown solid (182 mg, 94% yield over two steps); purification by silica gel column chromatography (cyclohexane/ethyl acetate, 6:4). Physical data identical to those of (2*R*,3*R*)-**5b**. $[\alpha]_D^{25} = +26$ ($c = 1.0$, CHCl_3). HPLC: Chiralcel OD-H, hexane/2-propanol (95:5), 1 mL/min, $\lambda = 254$ nm, t_R 75.68 min.

Methyl (2*R*,3*R*)-2-Benzoylamino-7-benzyloxy-3-hydroxyheptanoate [(2*R*,3*R*)-5b**]:** This compound was obtained from **4b** (0.5 mmol, 158 mg) by the General Procedure, by treatment with $[\text{Ru}(\text{R})\text{-SYNPHOS}^\text{®}\text{Br}_2]$, as a brown solid (179 mg, 93% yield over two steps); purification by silica gel column chromatography (cyclohexane/ethyl acetate, 6:4). M.p. 42 °C. ^1H NMR (CDCl_3 , 300 MHz): $\delta = 1.57$ (m, 6 H), 3.46 (t, $J = 6.1$ Hz, 2 H), 3.77 (s, 3 H), 4.04 (m, 1 H, CHOH), 4.48 (s, 2 H), 4.87 (dd, $J = 3.2$, 7.3 Hz, 1 H, CHNH), 7.28 (m, 5 H), 7.42 (t, $J = 7.0$ Hz, 2 H), 7.51 (t, $J = 7.2$ Hz, 1 H), 7.82 (d, $J = 7.0$ Hz, 2 H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz): $\delta = 22.5$, 29.4, 33.1, 52.6, 58.0, 70.1, 72.8, 3.0, 127.2, 127.5, 127.6, 128.3, 128.6, 131.9, 133.3, 138.4, 167.8, 170.9 ppm. MS (DCI, NH_3): m/z (%) = 386 (100) $[\text{M} + \text{H}]^+$ ppm. HRMS (DCI $^+$): m/z calcd. for $\text{C}_{22}\text{H}_{28}\text{NO}_5$: 386.1967; found 386.1971. $[\alpha]_D^{25} = -28$ ($c = 1.0$, CHCl_3). HPLC: Chiralcel OD-H, hexane/2-propanol (95:5), 1 mL/min, $\lambda = 254$ nm, t_R 50.89 min.

Methyl (2*S*,3*S*)-2-Benzoylamino-3-hydroxyoctanoate [(2*S*,3*S*)-5c**]:** This compound was obtained from **4c** (0.5 mmol, 112 mg) by the General Procedure, by treatment with $[\text{Ru}(\text{S})\text{-SYNPHOS}^\text{®}\text{Br}_2]$, as a brown solid (124 mg, 85% yield over two steps); purification by silica gel column chromatography (cyclohexane/ethyl acetate, 7:3). Physical data identical to those of (2*R*,3*R*)-**5c**. $[\alpha]_D^{25} = +26$ ($c = 1.0$, CHCl_3). HPLC: Chiralpak AS-H, hexane/2-propanol (98:2), 1.0 mL/min, $\lambda = 254$ nm, t_R 66.29 min.

Methyl (2*R*,3*R*)-2-Benzoylamino-3-hydroxyoctanoate [(2*R*,3*R*)-5c**]:** This compound was obtained from **4c** (0.5 mmol, 112 mg) by the General Procedure, by treatment with $[\text{Ru}(\text{R})\text{-SYNPHOS}^\text{®}\text{Br}_2]$, as a brown solid (132 mg, 90% yield over two steps); purification by silica gel column chromatography (cyclohexane/ethyl acetate, 7:3). M.p. 60 °C. ^1H NMR (CDCl_3 , 300 MHz): $\delta = 0.87$ (t, $J = 6.7$ Hz, 3 H), 1.28 (m, 4 H), 1.49 (m, 4 H), 3.80 (s, 3 H), 4.04 (m, 1 H, CHOH), 4.88 (dd, $J = 3.2$, 7.3 Hz, 1 H, CHNH), 7.24 (br. d, $J = 7.3$ Hz, 1 H, NH), 7.46 (m, 3 H), 7.82 (d, $J = 6.4$ Hz, 2 H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz): $\delta = 14.0$, 22.5, 25.3, 31.5, 33.4, 52.7, 58.0, 73.2, 127.2, 128.6, 131.9, 133.3, 167.9, 171.0 ppm. MS (DCI, NH_3): m/z (%) = 311 (2) $[\text{M} + \text{NH}_4]^+$, 294 (100) $[\text{M} + \text{H}]^+$ ppm. HRMS (DCI $^+$): m/z calcd. for $\text{C}_{16}\text{H}_{24}\text{NO}_4$: 294.1705; found 294.1711. $[\alpha]_D^{25} = -27$ ($c = 1.0$, CHCl_3). HPLC: Chiralpak AS-H, hexane/2-propanol (98:2), 1.0 mL/min, $\lambda = 254$ nm, t_R 50.83 min.

Methyl (2*S*,3*S*)-2-Benzoylamino-3-hydroxyoctadecanoate [(2*S*,3*S*)-5d**]:** This compound was obtained from **4d** (0.5 mmol, 182 mg) by the General Procedure, by treatment with $[\text{Ru}(\text{S})\text{-SYNPHOS}^\text{®}\text{Br}_2]$, as a slightly brown solid (180 mg, 83% yield over two steps); purification by silica gel column chromatography (cyclohexane/ethyl acetate, 8:2). M.p. 87 °C. ^1H NMR (CDCl_3 , 300 MHz): $\delta = 0.88$ (t, $J = 6.7$ Hz, 3 H), 1.25 (br. s, 26 H), 1.50 (m, 2 H), 3.83 (s, 3 H), 4.05 (m, 1 H, CHOH), 4.89 (dd, $J = 3.1$, 6.9 Hz, 1 H, CHNH), 7.15 (br. d, $J = 6.9$ Hz, 1 H, NH), 7.50 (m, 3 H), 7.84 (m, 2 H)

ppm. ^{13}C NMR (CDCl_3 , 75 MHz): $\delta = 14.1$, 22.7, 25.7, 29.7, 31.9, 33.4, 52.7, 58.1, 73.3, 127.2, 128.7, 130.1, 132.1, 167.9, 171.0 ppm. MS (DCI, NH_3): m/z (%) = 434 (100) $[\text{M} + \text{H}]^+$ ppm. HRMS (DCI $^+$): m/z calcd. for $\text{C}_{26}\text{H}_{44}\text{NO}_4$: 434.3270; found 434.3264. $[\alpha]_D^{25} = +19$ ($c = 0.8$, CHCl_3). HPLC: Chiralpak AS-H, hexane/2-propanol (98:2), 1.0 mL/min, $\lambda = 254$ nm, t_R 32.31 min.

Methyl (2*R*,3*R*)-2-Benzoylamino-3-hydroxyoctadecanoate [(2*R*,3*R*)-5d**]:** This compound was obtained from **4d** (0.5 mmol, 182 mg) by the General Procedure, by treatment with $[\text{Ru}(\text{R})\text{-SYNPHOS}^\text{®}\text{Br}_2]$, as a slightly brown solid (185 mg, 85% yield over two steps); purification by silica gel column chromatography (cyclohexane/ethyl acetate, 8:2). Physical data identical to those of (2*S*,3*S*)-**5d**. $[\alpha]_D^{25} = -22$ ($c = 0.8$, CHCl_3). HPLC: Chiralpak AS-H, hexane/2-propanol, (98:2), 1.0 mL/min, $\lambda = 254$ nm, $t_R = 26.37$ min.

Ethyl (2*S*,3*S*)-2-Benzoylamino-3-hydroxy-4-methylpentanoate [(2*S*,3*S*)-5e**]:** This compound was obtained from **4e** (0.5 mmol, 105 mg) by the General Procedure, by treatment with $[\text{Ru}(\text{S})\text{-SYNPHOS}^\text{®}\text{Br}_2]$, as a brown solid (125 mg, 90% yield over two steps); purification by silica gel column chromatography (cyclohexane/ethyl acetate, 8:2). Physical data identical to those of (2*R*,3*R*)-**5e**. $[\alpha]_D^{25} = +33$ ($c = 1.0$, CHCl_3). HPLC: Chiralcel OJ, hexane/2-propanol (96:04), 1.0 mL/min, $\lambda = 254$ nm, t_R 19.31 min.

Ethyl (2*R*,3*R*)-2-Benzoylamino-3-hydroxy-4-methylpentanoate [(2*R*,3*R*)-5e**]:** This compound was obtained from **4e** (0.5 mmol, 105 mg) by the General Procedure, by treatment with $[\text{Ru}(\text{R})\text{-SYNPHOS}^\text{®}\text{Br}_2]$, as a brown solid (135 mg, 96% yield over two steps); purification by silica gel column chromatography (cyclohexane/ethyl acetate, 8:2). M.p. 86 °C. ^1H NMR (CDCl_3 , 300 MHz): $\delta = 1.03$ (d, $J = 6.6$ Hz, 3 H), 1.06 (d, $J = 6.6$ Hz, 3 H), 1.34 (t, $J = 7.2$ Hz, 3 H), 1.79 (m, 1 H), 3.63 (dd, $J = 3.2$, 8.7 Hz, 1 H, CHOH), 4.28 (dq, $J = 1.9$, 7.2 Hz, 2 H), 4.93 (dd, $J = 3.1$, 7.2 Hz, 1 H, CHNH), 7.20 (br. d, $J = 7.2$ Hz, 1 H, NH), 7.47 (m, 3 H), 7.82 (m, 2 H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz): $\delta = 14.1$, 19.0, 31.6, 56.2, 61.9, 78.9, 127.1, 128.6, 131.9, 133.5, 167.5, 171.0 ppm. MS (DCI, NH_3): m/z (%) = 280 (100) $[\text{M} + \text{H}]^+$ ppm. HRMS (DCI $^+$): m/z calcd. for $\text{C}_{15}\text{H}_{22}\text{NO}_4$: 280.1549; found 280.1551. $[\alpha]_D^{25} = -36$ ($c = 1.0$, CHCl_3). HPLC: Chiralcel OJ, hexane/2-propanol (96:4), 1.0 mL/min, $\lambda = 254$ nm, t_R 15.82 min.

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