

K. Yin, E. Meggers



Paper

α -Amino Acid Synthesis by 1,3-Nitrogen Migration: An Update

Kuan Yin Eric Meggers*

Fachbereich Chemie, Philipps-Universität Marburg, Hans-Meerwein-Str. 4, 35043 Marburg, Germany meggers@chemie.uni-marburg.de



Received: 28.03.2024 Accepted after revision: 03.05.2024 Published online: 17.06.2024 (Version of Record) DOI: 10.1055/s-0043-1775371; Art ID: SS-2024-03-0105-OP

License terms: (cc) (i) (=) (\$

© 2024. The Author(s). This is an open access article published by Thieme under the terms of the Creative Commons Attribution-NonDerivative-NonCommercial-License, permitting copying and reproduction so long as the original work is given appropriate credit. Contents may not be used for commercial purposes or adapted, remixed, transformed or built upon. (https://creativecommons.org/licenses/by-nc-nd/4.0/)

Abstract An improved practical and efficient procedure for the synthesis of non-racemic unnatural α -amino acids through a stereocontrolled rearrangement is reported. Carboxylic acids are converted into azanyl esters RCO₂NHBoc followed by an iron-catalyzed 1,3-nitrogen migration to provide non-racemic α -amino acids in an asymmetric (α -monosubstituted α -amino acids) or enantioconvergent fashion (α , α -disubstituted α -amino acids). Under optimized conditions using a fluorinated chiral iron catalyst and 2,2,6,6-tetramethylpiperidine as the base in a solvent mixture of 1,2-dichlorobenzene and CHCl₃, enantiose-lectivities of up to 98% ee were obtained. Such high ee values are important for practical purposes, allowing the direct use of many of the obtained N-Boc-protected α -amino acids for subsequent applications.

Key words α -amino acids, asymmetric catalysis, iron, C(sp³)-H amination, rearrangements

Unnatural side-chain-carrying α -amino acids play pivotal roles in medicinal chemistry, biotechnology, chemical biology, and synthetic chemistry.¹ These non-native α -amino acids are incorporated into proteins and peptides to tailor their chemical, physical, or pharmaceutical properties. Additionally, they serve as chiral synthetic building blocks for producing chiral catalysts, chiral auxiliaries, and smallmolecule drugs. Numerous approaches for synthesizing non-racemic α -amino acids have been developed.^{2,3} However, there remains a significant demand for more efficient and economical methods. For example, catalytic asymmetric methods are generally more desirable than auxiliarymediated synthetic procedures but often do not provide the amino acids with sufficiently high enantiomeric purities, which prevents widespread implementation for use in academia and industry.

Recently, we introduced a convenient novel method to access non-racemic α -amino acids by a transition-metalcatalyzed 1,3-nitrogen rearrangement (Scheme 1).⁴ While our initial work disclosed a ruthenium- and iron-catalyzed synthesis of *N*-Troc-protected α -amino acids, we later revealed suitable reaction conditions for accessing more desirable *N*-Boc-protected α -amino acids through such ironcatalyzed 1,3-nitrogen shift.⁵ However, ee values were not high enough to be of real practical value. Herein, we report



Scheme 1 Catalytic asymmetric synthesis of α -amino acids by stereocontrolled 1,3-nitrogen migration: previous work and this study

K. Yin, E. Meggers

our progress in developing a highly practical and efficient catalytic asymmetric synthesis of α -amino acids with high enantiomeric excess.

We commenced our study with the screening of modified iron catalysts. Previously, we reported that (R,R)-[FeCl₂(**BIP**)], featuring a tetradentate bis-benzimidazole ligand with a chiral 2,2'-bipyrrolidine backbone (BIP) and two labile chloride ligands, hereafter denoted as (R,R)-FeBIP, emerged as a highly effective catalyst for stereocontrolled 1,3-nitrogen migration (see Table 1).⁴⁻⁶ We targeted the 5-position of the benzimidazole moiety for modification due to its proximity to the catalytic site without compromising the coordination ability of the tetradentate ligand. Utilizing the *N*-Boc-protected azanyl ester of phenylacetic acid (1) as the model substrate, (R,R)-FeBIP (2 mol%) in conjunction with the base 2,2,6,6-tetramethylpiperidine (TMP, 0.5 equiv) in 1,2-dichlorobenzene (DCB) converted 1 into N-Boc-phenylglycine (2) with 98% NMR yield and 90% ee, serving as our reference (entry 1). The introduction of a tert-butyl group at the 5-position of the benzimidazole moieties decreased the yield to 62% with 75% ee (entry 2). Similarly, the incorporation of electron-donating methoxy groups yielded no significant improvement (59% yield, 83% ee) (entry 3). However, an iron catalyst with nitro groups yielded 2 with 89% ee, albeit with a low NMR yield of just 37% (entry 4). Motivated by this high enantioselectivity, we explored other electron-withdrawing substituents at the 5-position of the benzimidazoles. Cyano groups provided 2 with an 66% NMR yield and 91% ee (entry 5), while chloride substituents afforded the same ee but a significantly improved yield (entry 6). The most favorable outcome was achieved with fluorine at the 5-position of the benzimidazoles (denoted as (*R*,*R*)-FeBIPF₂), catalyzing the 1,3-nitrogen migration with 85% NMR yield and 92% ee (entry 7). CF₃ groups were found to be less effective, providing 2 with only 71% NMR yield and 77% ee. We deduce from this catalyst screening that increased steric hindrance at the 5-position is unfavorable, whereas electron-withdrawing substituents enhance the enantiomeric excess of the rearrangement, with the small electron-withdrawing fluorine substituent seemingly offering optimal enantioselectivity.

With an improved iron catalyst in hand, our subsequent focus was on optimizing the reaction conditions. Notably, we found that the reaction temperature influenced the enantioselectivity significantly. For instance, employing the rearrangement of $\mathbf{1} \rightarrow \mathbf{2}$ as the model reaction, we observed an enantiomeric excess (ee) of just 89% at room temperature (Table 2, entry 1), which is significantly lower than the 92% ee observed at 0 °C (entry 2, also refer to Table 1, entry 7). Further lowering the reaction temperature to -10 °C enhanced the enantioselectivity to 94% ee (entry 3). However, due to the high melting point of DCB (-17 °C), additional reduction of the reaction temperature in this solvent was impractical. Consequently, we explored CHCl₃ as an alternaPaper



2671

THIEME



^a Reaction conditions: Substrate (0.2 mmol), Fe catalyst (2.0 mol%), TMP (0.1 mmol) in DCB (2.0 mL) were stirred for 16 h at 0 °C under an atmosphere of nitrogen. TMP = 2,2,6,6-tetramethylpiperidine, DCB = 1,2-dichlorobenzene.

^b Determined by ¹H NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard.

^c Determined by HPLC analysis on a chiral stationary phase.

tive, but this yielded inferior results compared to those with DCB (entry 4). However, a mixture of DCB and CHCl₃ (1:1) emerged as a viable option, yielding the same enantioselectivity of 94% ee as pure DCB at -15 °C (entry 5). Further reducing the temperature to -30 °C improved the enantioselectivity to 95% ee. However, at these lower temperatures, yields were unsatisfactory due to low conversions (compare entries 1 and 2 with entries 3–6). This challenge was addressed by accelerating the reaction with an increased amount of base. Doubling the amount of TMP from 0.5 to 1.0 equivalent led to an enhanced NMR yield of 93% and a slight improvement of the enantiomeric excess to 96% ee at -30 °C (entry 7). Ultimately, optimal results were achieved in DCB/CHCl₃ (1:1) at -50 °C using 2.0 equivalents of TMP, yielding the rearranged amino acid in 98% NMR yield and 98% ee (entry 8).

Next, we applied the new catalyst and optimized conditions to various substrates (Scheme 2). Azanyl ester substrates were easily obtained in a single step by DCC-mediated coupling of abundant carboxylic acids with *N*-Boc-protected hydroxylamine (BocNHOH). These azanyl esters, RCO₂NHBoc, were then subjected to the stereocontrolled (*R*,*R*)-**FeBIPF**₂-catalyzed 1,3-nitrogen migration. Initially, reactions were conducted at -30 °C.



2672

OPEN





^a Reaction conditions: Substrate (0.2 mmol), (*R*,*R*)-FeBIPF₂ (2.0 mol%), TMP (0.1 or 0.2 mmol) in DCB or DCB/CHCl₃ (1:1) (2.0 mL) were stirred for 16 h at the indicated temperature under an atmosphere of nitrogen. TMP 2,2,6,6-tetramethylpiperidine, DCB = 1,2-dichlorobenzene.

2.0

98

98

-50

^b Determined by ¹H NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard

^c Determined by HPLC analysis on a chiral stationary phase.

8

DCB/CHCl₃(1:1)

Azanyl esters with diverse substituents in the phenyl ring yielded rearranged N-Boc-phenylglycine derivatives 3-11 in 81–97% isolated yield and with 88–96% ee. The highest enantioselectivities (at -30 °C) were observed for N-Boc-phenylglycine bearing a cyano group in the para-position (3, 96% ee) or two CF_3 groups in the *meta*-positions (10, 96% ee), while the lowest enantioselectivity was obtained for *N*-Boc-phenylglycine with a chlorine substituent in the ortho-position of the phenyl moiety (7, 88% ee).

Subsequently, we applied the new reaction conditions to the catalytic enantioconvergent⁷ synthesis of non-racemic α, α -disubstituted α -amino acids from racemic α branched azanyl esters, yielding amino acids 12-24 in 81-93% yield and with 78-97% ee. Particularly high enantioselectivities were achieved in the rearrangements to α,α disubstituted α -phenylglycines bearing a cyclopentyl (22, 96% ee) or cyclohexyl (23, 97% ee) substituent in the α -position.

Lastly, it is noteworthy that enantioselectivities could be slightly enhanced by reducing the reaction temperature from -30 to -50 °C, as already demonstrated for the model reaction $1 \rightarrow 2$ (Table 2, entries 7 and 8), and this trend held true for the formation of 12 (96% ee at -50 °C vs. 95% ee at -30 °C) and 23 (98% ee at -50 °C vs. 97% ee at -30 °C).

In conclusion, we here provided an update on our recently introduced method to synthesize non-racemic unnatural α-amino acids by iron-catalyzed stereocontrolled rearrangement of azanayl esters RCO₂NHBoc into Boc-protected α -amino acids. Through the optimization of the iron catalyst by fluorination of the benzimidazole moieties, along with adjustments to the solvent and reaction tem-

Paper



Scheme 2 Substrate scope. Reagents and conditions: Substrate (0.2 mmol), (R,R)-FeBIPF₂ (2.0 or 5.0 mol%), TMP (0.2 mmol) in DCB/CHCl₃ (1:1) (2.0 mL) were stirred for 16-40 h at -30 °C under an atmosphere of nitrogen. Isolated yields are provided. Catalyst loading: 2.0 mol% for α -monosubstituted α -amino acids, 5.0 mol% for α , α -disubstituted α -amino acids. ^a At -50 °C with 2.0 equiv of TMP.



perature, we have achieved significantly enhanced enantioselectivities, reaching up to 98% ee for the synthesis of α monosubstituted and α, α -disubstituted *N*-Boc-protected α amino acids. These high enantiomeric excess values are crucial for practical applications, as they enable the direct utilization of many of the obtained *N*-Boc-protected α -amino acids in subsequent processes.

Catalytic reactions were performed in Schlenk tubes (10 mL) under a nitrogen atmosphere with magnetic stirring. Chemicals were used as received from commercial suppliers unless stated otherwise. Anhydrous CHCl₃, CH₃CN, and CH₂Cl₂ were distilled under nitrogen from calcium hydride. Anhydrous THF was distilled under nitrogen from sodium/benzophenone. Anhydrous 1,2-dichlorobenzene was used as received from commercial suppliers. Flash column chromatography was performed with silica gel 60 M from Macherey-Nagel (230-400 mesh). ¹H, ¹³C, and ¹⁹F NMR spectra were recorded with a Bruker Avance 300 MHz spectrometer at ambient temperature. Chemical shifts are expressed in parts per million (δ) referenced to chloroform (7.26 ppm or 77.23 ppm) or MeOH (3.31 ppm or 49.15 ppm). Highresolution mass spectra (HRMS) were recorded with a Bruker En Apex Ultra 7.0 T FT-MS mass spectrometer. Optical rotations were measured with a Perkin–Elmer 241 polarimeter with $[\alpha]_{D}^{25}$ values reported in degrees and concentrations reported in g/100 mL. Enantiomeric excess values were determined by HPLC analysis on chiral stationary phases with an Agilent HPLC 1260.

Synthesis of Azanyl Ester Substrates; General Procedure⁴

To a solution of carboxylic acid (1.0 equiv) and N-protected hydroxylamine (1.0 equiv) in dichloromethane (0.2 M) at 0 °C was added dropwise a solution of *N*,*N'*-dicyclohexylcarbodiimide (DCC, 1.0 equiv) in CH₂Cl₂ (1.0 mol/L). The reaction mixture was warmed to room temperature and stirred for 2 hours. After completion, the reaction mixture was filtered and washed with a small amount of CH₂Cl₂. After concentration under reduced pressure, the residue was purified by chromatography on silica gel.

tert-Butyl (2-(4-Cyanophenyl)acetoxy)carbamate

From 2-(4-cyanophenyl)acetic acid (242 mg, 1.5 mmol) and *tert*-butyl hydroxycarbamate (200 mg, 1.5 mmol) coupled with DCC (309 mg, 1.5 mmol) and obtained as a colorless oil (chromatography on silica gel, eluent: EtOAc/hexane = 1:5).

Yield: 383 mg (92%).

¹H NMR (300 MHz, CDCl₃): δ = 7.87 (s, 1 H), 7.65 (d, *J* = 8.4 Hz, 2 H), 7.44 (d, *J* = 8.0 Hz, 2 H), 3.84 (s, 2 H), 1.47 (s, 9 H).

¹³C NMR (75 MHz, CDCl₃): δ = 169.90, 155.39, 137.71, 132.74, 130.44, 118.68, 112.01, 83.89, 38.83, 28.21.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₁₄H₁₆N₂O₄Na: 299.1002; found: 299.1000.

tert-Butyl (2-(4-(Methylthio)phenyl)acetoxy)carbamate

From 2-(4-(methylthio)phenyl)acetic acid (364 mg, 2.0 mmol) and *tert*-butyl hydroxycarbamate (266 mg, 2.0 mmol) coupled with DCC (413 mg, 2.0 mmol) and obtained as a colorless oil (chromatography on silica gel, eluent: EtOAc/hexane = 1:5).

Yield: 555 mg (93%).

¹H NMR (300 MHz, CDCl₃): δ = 7.93 (d, *J* = 7.4 Hz, 1 H), 7.22 (s, 4 H), 3.72 (s, 2 H), 2.46 (s, 3 H), 1.46 (s, 9 H).

Paper

 ^{13}C NMR (75 MHz, CDCl_3): δ = 170.92, 155.59, 138.14, 129.96, 129.18, 127.13, 83.55, 38.29, 28.18, 16.02.

HRMS (ESI): $m/z \ [M + Na]^+$ calcd for $C_{14}H_{19}NO_4Na$: 320.0927; found: 320.0923.

tert-Butyl (2-(4-(tert-Butoxy)phenyl)acetoxy)carbamate

From 2-(4-(*tert*-butoxy)phenyl)acetic acid (625 mg, 3.0 mmol) and *tert*-butyl hydroxycarbamate (399 mg, 3.0 mmol) coupled with DCC (619 mg, 3.0 mmol) and obtained as a colorless oil (chromatography on silica gel, eluent: EtOAc/hexane = 1:5).

Yield: 856 mg (88%).

¹H NMR (300 MHz, CDCl₃): δ = 7.91 (s, 1 H), 7.19 (d, J = 7.2 Hz, 2 H), 6.94 (d, J = 6.8 Hz, 2 H), 3.71 (s, 2 H), 1.45 (s, 9 H), 1.33 (s, 9 H).

 ^{13}C NMR (75 MHz, CDCl_3): δ = 171.16, 155.63, 155.06, 130.01, 127.19, 124.49, 83.48, 78.77, 38.16, 29.01, 28.19.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₁₇H₂₅NO₅Na: 346.1625; found: 346.1621.

tert-Butyl (2-(2-Fluorophenyl)acetoxy)carbamate

From 2-(2-fluorophenyl)acetic acid (308 mg, 2.0 mmol) and *tert*-butyl hydroxycarbamate (266 mg, 2.0 mmol) coupled with DCC (413 mg, 2.0 mmol) to obtain a colorless oil (chromatography on silica gel, eluent: EtOAc/hexane = 1:5).

Yield: 474 mg (88%).

¹H NMR (300 MHz, CDCl₃): δ = 7.91 (d, J = 9.4 Hz, 1 H), 7.30 (q, J = 6.5, 5.6 Hz, 2 H), 7.18 – 7.02 (m, 2 H), 3.82 (s, 2 H), 1.47 (s, 9 H).

¹³C NMR (75 MHz, CDCl₃): δ = 170.26, 161.19 (d, *J* = 245.25 Hz), 155.56, 131.66 (d, *J* = 3.75 Hz), 129.82 (d, *J* = 8.25 Hz), 124.54 (d, *J* = 3.75 Hz), 119.91 (d, *J* = 15.75 Hz), 115.73 (d, *J* = 21.75 Hz), 83.60, 32.18 (d, *J* = 3.75 Hz), 28.19.

¹⁹F NMR (282 MHz, CDCl₃): δ = -116.83.

HRMS (ESI): m/z [M + Na]⁺ calcd C₁₃H₁₆FNO₄Na: 292.0956; found: 292.0951.

tert-Butyl (2-(2-Chlorophenyl)acetoxy)carbamate

From 2-(2-chlorophenyl)acetic acid (341 mg, 2.0 mmol) and *tert*-butyl hydroxycarbamate (266 mg, 2.0 mmol) coupled with DCC (413 mg, 2.0 mmol) and obtained as a colorless oil (chromatography on silica gel, eluent: EtOAc/hexane = 1:5).

Yield: 445 mg (78%).

¹H NMR (300 MHz, CDCl₃): δ = 7.90 (s, 1 H), 7.46–7.33 (m, 2 H), 7.28 (t, *J* = 3.1 Hz, 2 H), 3.95 (s, 2 H), 1.50 (s, 9 H).

 ^{13}C NMR (75 MHz, CDCl₃): δ = 170.19, 155.56, 134.75, 131.73, 130.93, 129.85, 129.43, 127.34, 83.61, 36.79, 28.23.

HRMS (ESI): $m/z \ [M + Na]^+$ calcd $C_{13}H_{16}CINO_4Na$: 308.0660; found: 308.0656.

tert-Butyl (2-(2,4-Difluorophenyl)acetoxy)carbamate

From 2-(2,4-difluorophenyl)acetic acid (344 mg, 2.0 mmol) and *tert*butyl hydroxycarbamate (266 mg, 2.0 mmol) coupled with DCC (413 mg, 2.0 mmol) and obtained as a colorless oil (chromatography on silica gel, eluent: EtOAc/hexane = 1:5).

Yield: 512 mg (89%).

		THIEME
Syn <mark>thesis</mark>	K. Yin, E. Meggers	OPEN ACCESS

¹H NMR (300 MHz, CDCl₃): δ = 7.89 (s, 1 H), 7.30 (t, *J* = 7.8 Hz, 1 H), 6.84 (t, *J* = 8.7 Hz, 2 H), 3.78 (s, 2 H), 1.47 (s, 9 H).

¹³C NMR (75 MHz, CDCl₃): δ = 170.00, 162.73 (dd, *J* = 247.5, 11.25 Hz), 161.16 (dd, *J* = 248.25, 11.25 Hz), 155.59, 132.33 (dd, *J* = 9.75, 5.25 Hz), 115.90 (dd, *J* = 15.75, 3.75 Hz), 111.66 (dd, *J* = 21.00 Hz, 3.75 Hz), 104.13 (t, *J* = 25.50 Hz), 83.51, 31.50 (d, *J* = 3.00 Hz), 28.10.

 ^{19}F NMR (282 MHz, CDCl₃): δ = –110.30 (d, J = 7.6 Hz), –112.35 (d, J = 7.5 Hz).

HRMS (ESI): *m*/*z* [M + Na]⁺ calcd for C₁₃H₁₅F₂NO₄Na: 310.0861; found: 310.0856.

tert-Butyl (2-(2,6-Dichlorophenyl)acetoxy)carbamate

From 2-(2,6-dichlorophenyl)acetic acid (410 mg, 2.0 mmol) and *tert*butyl hydroxycarbamate (266 mg, 2.0 mmol) coupled with DCC (413 mg, 2.0 mmol) and obtained as a colorless oil (chromatography on silica gel, eluent: EtOAc/hexane = 1:5).

Yield: 587 mg (92%).

¹H NMR (300 MHz, CDCl₃): δ = 7.86 (s, 1 H), 7.35 (d, J = 8.1 Hz, 2 H), 7.20 (t, J = 8.0 Hz, 1 H), 4.17 (s, 2 H), 1.48 (s, 9 H).

¹³C NMR (75 MHz, CDCl₃): δ = 169.19, 155.46, 136.43, 129.81, 129.69, 128.41, 83.62, 34.63, 28.23.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₁₃H₁₅Cl₂NO₄Na: 342.0270; found: 342.0266.

tert-Butyl (2-(3,5-Bis(trifluoromethyl)phenyl)acetoxy)carbamate

From 2-(3,5-bis(trifluoromethyl)phenyl)acetic acid (341 mg, 1.5 mmol) and *tert*-butyl hydroxycarbamate (200 mg, 1.5 mmol) coupled with DCC (309 mg, 1.5 mmol) and obtained as a colorless oil (chromatography on silica gel, eluent: EtOAc/hexane = 1:3).

Yield: 487 mg (84%).

¹H NMR (300 MHz, CDCl₃): δ = 7.89 (s, 1 H), 7.81 (d, *J* = 10.0 Hz, 3 H), 3.91 (s, 2 H), 1.47 (s, 9 H).

¹³C NMR (75 MHz, CDCl₃): δ = 169.71, 155.47, 134.89, 132.31 (q, *J* = 33.75 Hz), 129.94, 123.32 (q, *J* = 270.00 Hz), 121.97 (m), 83.96, 38.23, 28.13.

¹⁹F NMR (282 MHz, CDCl₃): δ = -62.94.

HRMS (ESI): $m/z \,[M + Na]^+$ calcd for $C_{15}H_{15}F_6NO_4Na$: 410.0797; found: 410.0795.

tert-Butyl (2-(3,5-Dimethoxyphenyl)acetoxy)carbamate

From 2-(3,5-dimethoxyphenyl)acetic acid (392 mg, 2.0 mmol) and *tert*-butyl hydroxycarbamate (266 mg, 2.0 mmol) coupled with DCC (413 mg, 2.0 mmol) and obtained as a colorless oil (chromatography on silica gel, eluent: EtOAc/hexane = 1:6).

Yield: 592 mg (95%).

¹H NMR (300 MHz, CDCl₃): δ = 7.91 (s, 1 H), 6.46 (d, *J* = 2.2 Hz, 2 H), 6.38 (t, *J* = 2.3 Hz, 1 H), 3.78 (s, 6 H), 3.69 (s, 2 H), 1.46 (s, 9 H).

 ^{13}C NMR (75 MHz, CDCl_3): δ = 170.80, 161.18, 155.59, 134.47, 107.56, 99.96, 83.54, 55.55, 39.08, 28.19.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₁₅H₂₁NO₆Na: 334.1261; found: 334.1255.

tert-Butyl ((2-([1,1'-Biphenyl]-4-yl)propanoyl)oxy)carbamate

From 2-([1,1'-biphenyl]-4-yl)propanoic acid (341 mg, 1.0 mmol) and *tert*-butyl hydroxycarbamate (133 mg, 1.0 mmol) coupled with DCC

(206 mg, 1.0 mmol) and obtained as a colorless oil (chromatography on silica gel, eluent: EtOAc/hexane = 1:10).

Yield: 303 mg (89%).

2674

¹H NMR (300 MHz, CDCl₃): δ = 7.79 (s, 1 H), 7.57 (d, *J* = 7.4 Hz, 4 H), 7.48–7.39 (m, 4 H), 7.38–7.31 (m, 1 H), 3.94 (q, *J* = 7.2 Hz, 1 H), 1.63 (d, *J* = 7.2 Hz, 3 H), 1.45 (s, 9 H).

 ^{13}C NMR (75 MHz, CDCl_3): δ = 174.30, 155.65, 140.73, 140.67, 138.01, 128.90, 128.16, 127.61, 127.48, 127.16, 83.22, 43.16, 27.61, 18.60.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₂₀H₂₃NO₄Na: 364.1519; found: 364.1512.

tert-Butyl ((2-(3-Benzoylphenyl)propanoyl)oxy)carbamate

From 2-(3-benzoylphenyl)propanoic acid (509 mg, 2.0 mmol) and *tert*-butyl hydroxycarbamate (266 mg, 2.0 mmol) coupled with DCC (413 mg, 2.0 mmol) and obtained as a colorless oil (chromatography on silica gel, eluent: EtOAc/hexane = 1:5).

Yield: 704 mg (95%).

¹H NMR (300 MHz, CDCl₃): δ = 7.91 (s, 1 H), 7.79 (d, *J* = 7.3 Hz, 3 H), 7.69 (d, *J* = 7.6 Hz, 1 H), 7.58 (d, *J* = 6.9 Hz, 2 H), 7.46 (q, *J* = 7.3 Hz, 3 H), 3.95 (q, *J* = 7.2 Hz, 1 H), 1.61 (d, *J* = 7.2 Hz, 3 H), 1.43 (s, 9 H).

 ^{13}C NMR (75 MHz, CDCl₃): δ = 196.42, 173.52, 155.54, 139.35, 138.20, 137.50, 132.71, 131.77, 130.22, 129.54, 129.40, 128.89, 128.48, 83.36, 43.41, 27.68, 18.64.

HRMS (ESI): $m/z \ [M + Na]^+$ calcd for $C_{21}H_{23}NO_5Na$: 392.1468; found: 392.1465.

tert-Butyl ((2-(Benzo[d][1,3]dioxol-5-yl)propanoyl)oxy)carbamate

From 2-(benzo[*d*][1,3]dioxol-5-yl)propanoic acid (213 mg, 1.1 mmol) and *tert*-butyl hydroxycarbamate (146 mg, 1.1 mmol) coupled with DCC (227 mg, 1.1 mmol) and obtained as a colorless oil (chromatography on silica gel, eluent: EtOAc/hexane = 1:10).

Yield: 248 mg (73%).

¹H NMR (300 MHz, CDCl₃): δ = 7.78 (s, 1 H), 6.84 (s, 1 H), 6.81–6.73 (m, 2 H), 5.94 (s, 2 H), 3.80 (q, *J* = 7.2 Hz, 1 H), 1.54 (d, *J* = 7.2 Hz, 3 H), 1.45 (s, 9 H).

 ^{13}C NMR (75 MHz, CDCl₃): δ = 174.06, 155.63, 148.16, 147.27, 132.75, 121.19, 108.63, 108.21, 101.35, 83.49, 43.24, 28.20, 18.83.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₁₅H₁₉NO₆Na: 332.1105; found: 332.1096.

tert-Butyl ((2-(Naphthalen-2-yl)propanoyl)oxy)carbamate

From 2-(naphthalen-2-yl)propanoic acid (200 mg, 1.0 mmol) and *tert*-butyl hydroxycarbamate (133 mg, 1.0 mmol) coupled with DCC (206 mg, 1.0 mmol) and obtained as a colorless oil (chromatography on silica gel, eluent: EtOAc/hexane = 1:9).

Yield: 271 mg (86%).

¹H NMR (300 MHz, CDCl₃): δ = 7.90–7.71 (m, 5 H), 7.56–7.38 (m, 3 H), 4.06 (q, J = 7.2 Hz, 1 H), 1.69 (d, J = 7.1 Hz, 3 H), 1.43 (s, 9 H).

 ^{13}C NMR (75 MHz, CDCl₃): δ = 174.05, 155.63, 136.42, 133.64, 132.99, 128.78, 128.06, 127.84, 126.69, 126.51, 126.28, 125.75, 83.46, 43.75, 28.17, 18.70.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₁₈H₂₁NO₄Na: 338.1363; found: 338.1358.

C			
SV/h	TI	1 D C I	
		LC3	

K. Yin, E. Meggers

tert-Butyl ((2-(Naphthalen-1-yl)propanoyl)oxy)carbamate

From 2-(naphthalen-1-yl)propanoic acid (200 mg, 1.0 mmol) and *tert*-butyl hydroxycarbamate (133 mg, 1.0 mmol) coupled with DCC (206 mg, 1.0 mmol) and obtained as a colorless oil (chromatography on silica gel, eluent: EtOAc/hexane = 1:9).

Yield: 288 mg (91%).

¹H NMR (300 MHz, CDCl₃): δ = 8.08 (d, *J* = 8.4 Hz, 1 H), 7.93–7.73 (m, 3 H), 7.59–7.42 (m, 4 H), 4.70 (q, *J* = 7.0 Hz, 1 H), 1.75 (d, *J* = 7.1 Hz, 3 H), 1.42 (s, 9 H).

 ^{13}C NMR (75 MHz, CDCl₃): δ = 174.45, 155.65, 135.15, 134.21, 131.35, 129.27, 128.47, 126.81, 125.99, 125.76, 125.00, 123.02, 83.43, 39.42, 28.17, 18.32.

HRMS (ESI): $m/z [M + Na]^+$ calcd for $C_{18}H_{21}NO_4Na$: 338.1363; found: 338.1356.

tert-Butyl ((2-(Thiophen-3-yl)propanoyl)oxy)carbamate

From 2-(thiophen-3-yl)propanoic acid (156 mg, 1.0 mmol) and *tert*butyl hydroxycarbamate (133 mg, 1.0 mmol) coupled with DCC (206 mg, 1.0 mmol) and obtained as a colorless oil (chromatography on silica gel, eluent: EtOAc/hexane = 1:10).

Yield: 236 mg (87%).

¹H NMR (300 MHz, CDCl₃): δ = 7.88 (s, 1 H), 7.29 (dd, J = 5.0, 2.9 Hz, 1 H), 7.21 (s, 1 H), 7.09 (d, J = 4.8 Hz, 1 H), 4.00 (q, J = 7.2 Hz, 1 H), 1.59 (d, J = 7.2 Hz, 3 H), 1.45 (s, 9 H).

¹³C NMR (75 MHz, CDCl₃): δ = 173.63, 155.63, 139.01, 127.16, 126.22, 122.11, 83.44, 39.07, 28.17, 18.38.

HRMS (ESI): m/z [M + Na]⁺ for $C_{12}H_{17}NO_4SNa$: 294.0770; found: 294.0764.

tert-Butyl (2-Cyclopentyl-2-phenylacetoxy)carbamate

From 2-cyclopentyl-2-phenylacetic acid (408 mg, 2.0 mmol) and *tert*butyl hydroxycarbamate (266 mg, 2.0 mmol) coupled with DCC (413 mg, 2.0 mmol) and obtained as a colorless oil (chromatography on silica gel, eluent: EtOAc/hexane = 1:10).

Yield: 558 mg (87%).

¹H NMR (300 MHz, $CDCl_3$): δ = 7.75 (s, 1 H), 7.44–7.26 (m, 5 H), 3.44 (d, *J* = 11.1 Hz, 1 H), 2.61 (dq, *J* = 15.8, 8.2 Hz, 1 H), 1.96 (ddd, *J* = 15.1, 7.4, 3.8 Hz, 1 H), 1.75–1.58 (m, 3 H), 1.55–1.45 (m, 2 H), 1.42 (s, 9 H), 1.38–1.30 (m, 1 H), 1.12–0.97 (m, 1 H).

 ^{13}C NMR (75 MHz, CDCl₃): δ = 173.54, 155.64, 137.69, 128.87, 128.56, 127.84, 83.35, 55.57, 43.73, 31.62, 30.98, 28.16, 25.36, 24.97.

HRMS (ESI): $m/z \,[M + Na]^*$ calcd for $C_{18}H_{25}NO_4Na$: 342.1676; found: 342.1667.

tert-Butyl (2-Cyclohexyl-2-phenylacetoxy)carbamate

From 2-cyclohexyl-2-phenylacetic acid (436 mg, 2.0 mmol) and *tert*butyl hydroxycarbamate (266 mg, 2.0 mmol) coupled with DCC (413 mg, 2.0 mmol) and obtained as a colorless oil (chromatography on silica gel, eluent: EtOAc/hexane = 1:10).

Yield: 521 mg (78%).

¹H NMR (300 MHz, CDCl₃): δ = 7.74 (s, 1 H), 7.41–7.25 (m, 5 H), 3.38 (d, *J* = 10.5 Hz, 1 H), 2.20–1.97 (m, 1 H), 1.90 (d, *J* = 12.2 Hz, 1 H), 1.76 (d, *J* = 14.2 Hz, 1 H), 1.68–1.59 (m, 2 H), 1.41 (s, 9 H), 1.29 (d, *J* = 20.9 Hz, 2 H), 1.20–1.06 (m, 3 H), 0.88–0.64 (m, 1 H).

 ^{13}C NMR (75 MHz, CDCl₃): δ = 173.44, 155.62, 136.57, 128.84, 128.80, 127.80, 83.26, 56.50, 41.38, 31.95, 30.54, 28.11, 26.37, 26.31, 26.05.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₁₉H₂₇NO₄Na: 356.1832; found: 356.1825.

tert-Butyl ((1,2,3,4-Tetrahydronaphthalene-1-carbonyl)oxy)carbamate

From 1,2,3,4-tetrahydronaphthalene-1-carboxylic acid (352 mg, 2.0 mmol) and *tert*-butyl hydroxycarbamate (266 mg, 2.0 mmol) coupled with DCC (413 mg, 2.0 mmol) and obtained as a colorless oil (chromatography on silica gel, eluent: EtOAc/hexane = 1:10).

Yield: 480 mg (82%).

 ^1H NMR (300 MHz, CDCl₃): δ = 7.86 (s, 1 H), 7.25–7.03 (m, 4 H), 4.01 (t, J = 5.9 Hz, 1 H), 2.94–2.67 (m, 2 H), 2.29–1.93 (m, 3 H), 1.92–1.74 (m, 1 H), 1.49 (s, 9 H).

 ^{13}C NMR (75 MHz, CDCl₃): δ = 174.56, 155.73, 137.56, 131.91, 129.78, 129.65, 127.52, 126.23, 83.47, 42.95, 29.15, 28.25, 26.84, 20.63.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₁₆H₂₁NO₄Na: 314.1363; found: 314.1353.

Amino Acid Synthesis; General Procedure

To a Schlenk tube (10 mL) was added the substrate (0.2 mmol) and (R,R)-**FeBIPF**₂ (2–5 mol%). The tube was evacuated and backfilled with N₂ three times. A mixture of 1,2-dichlorobenzene (DCB, 1.0 mL) and CHCl₃ (1.0 mL) was added, and the mixture was degassed five times via freeze-pump-thaw. 2,2,6,6-Tetramethylpiperidine (TMP, 0.1–0.4 mmol) was added under N₂ atmosphere and the Schlenk tube was sealed. The reaction mixture was stirred at the indicated temperature for 16–40 hours. To quench the reaction, aqueous NaHSO₄ solution (2 M, 10 mL) was added, and the mixture was extracted with CH₂Cl₂ (3 × 15 mL). The combined organic layer was dried over anhydrous sodium sulfate. After filtration, the solvent was evaporated under reduced pressure, and the residue was purified by column chromatography on silica gel using the indicated solvent as the eluent. Enantiomeric ratios were determined by HPLC analysis on a chiral stationary phase.

(S)-2-((tert-Butoxycarbonyl)amino)-2-phenylacetic Acid (2)

From *tert*-butyl (2-phenylacetoxy)carbamate⁵ (50.2 mg, 0.2 mmol) using (*R*,*R*)-**FeBIPF₂** (2 mol%) and TMP (0.4 mmol, 68 μ L) at –50 °C for 16 h. Flash column chromatography on silica gel with *n*-hexane/EtOAc (6:1, plus 0.2% HOAc) as the eluent provided **2** as a colorless gum (49.1 mg, 98% yield, 98% ee).

HPLC analysis for determining the ee value: Daicel Chiralpak IG column, 250 × 4.6 mm, mobile phase *n*-hexane/*i*PrOH = 9:1 (v/v) with 0.1% TFA, flow rate 1.0 mL/min, UV detection at 210 nm, 25 °C; t_1 = 14.5 min, t_2 = 21.1 min.

 $[\alpha]_D^{25}$ +100.4 (*c* 1.0, MeOH).

Analytical data are consistent with a recent report.5

(S)-2-((*tert*-Butoxycarbonyl)amino)-2-(4-cyanophenyl)acetic Acid (3)

From *tert*-butyl (2-(4-cyanophenyl)acetoxy)carbamate (55.3 mg, 0.2 mmol) using (R,R)-**FeBIPF**₂ (2 mol%) and TMP (0.2 mmol, 34 µL) at -30 °C for 16 h. Flash column chromatography on silica gel with n-hexane/EtOAc (5:1, plus 0.2% HOAc) as the eluent provided **3** as a colorless gum (49.2 mg, 89% yield, 96% ee).

HPLC analysis for determining the ee value: Daicel Chiralpak IG column, 250 × 4.6 mm, mobile phase *n*-hexane/*i*PrOH = 4:1 (v/v) with 0.1% TFA, flow rate 1.0 mL/min, UV detection at 210 nm, 25 °C; t_1 = 8.3 min, t_2 = 12.5 min.

THIEME OPEN

2676

K. Yin, E. Meggers

THIEME OPEN ACCESS

 $[\alpha]_D^{25}$ +99.9 (*c* 1.0, MeOH).

¹H NMR (300 MHz, CD₃OD): δ = 7.42 (q, *J* = 4.0 Hz, 2 H), 7.35–7.20 (m, 2 H), 5.68 (s, 1 H), 1.44 (s, 9 H).

 ^{13}C NMR (75 MHz, CD₃OD): δ = 172.95, 157.44, 144.80, 133.64, 129.69, 119.60, 113.04, 81.19, 59.03, 28.78.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₁₄H₁₆N₂O₄Na: 299.1002; found: 299.0992.

(S)-2-((*tert*-Butoxycarbonyl)amino)-2-(4-(methylthio)phenyl)acetic Acid (4)

From *tert*-butyl (2-(4-(methylthio)phenyl)acetoxy)carbamate (59.5 mg, 0.2 mmol) using (*R*,*R*)-**FeBIPF**₂ (2 mol%) and TMP (0.2 mmol, 34 μ L) at -30 °C for 16 h. Flash column chromatography on silica gel with *n*-hexane/EtOAc (5:1, plus 0.2% HOAc) as the eluent provided **4** as a colorless gum (56.2 mg, 94% yield, 95% ee).

HPLC analysis for determining the ee value: Daicel Chiralpak IG column, 250 × 4.6 mm, mobile phase *n*-hexane/iPrOH = 4:1 (v/v) with 0.1% TFA, flow rate 1.0 mL/min, UV detection at 210 nm, 25 °C; t_1 = 10.5 min, t_2 = 13.2 min.

[α]_D²⁵ +133.7 (*c* 1.0, MeOH).

¹H NMR (300 MHz, CD₃OD): δ = 7.32 (d, *J* = 6.0 Hz, 2 H), 7.24 (d, *J* = 6.1 Hz, 2 H), 5.18 (s, 1 H), 2.43 (s, 3 H), 1.38 (s, 9 H).

 ^{13}C NMR (75 MHz, CD₃OD): δ = 174.27, 157.58, 140.43, 135.46, 129.18, 127.74, 80.97, 58.90, 28.83, 15.74.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₁₄H₁₉NO₄SNa: 320.0927; found: 320.0921.

(S)-2-(4-(*tert*-Butoxy)phenyl)-2-((*tert*-butoxycarbonyl)amino)acetic Acid (5)

From *tert*-butyl (2-(4-(*tert*-butoxy)phenyl)acetoxy)carbamate (64.7 mg, 0.2 mmol) using (R,R)-**FeBIPF**₂ (2 mol%) and TMP (0.2 mmol, 34 μ L) at -30 °C for 16 h. Flash column chromatography on silica gel with *n*-hexane/EtOAc (5:1, plus 0.2% HOAc) as the eluent provided **5** as a colorless gum (62.7 mg, 97% yield, 92% ee).

HPLC analysis for determining the ee value: Daicel Chiralpak IG column, 250 × 4.6 mm, mobile phase *n*-hexane/iPrOH = 9:1 (v/v) with 0.1% TFA, flow rate 1.0 mL/min, UV detection at 210 nm, 25 °C; t_1 = 12.4 min, t_2 = 18.9 min.

 $[\alpha]_{D}^{25}$ +122.3 (*c* 1.0, MeOH).

¹H NMR (300 MHz, CD₃OD): δ = 7.38–7.30 (m, 2 H), 7.01 (d, *J* = 8.6 Hz, 2 H), 5.19 (s, 1 H), 1.47 (s, 9 H), 1.36 (s, 9 H).

¹³C NMR (75 MHz, CD₃OD): δ = 174.50, 157.57, 156.77, 133.64, 129.36, 125.30, 80.92, 79.89, 58.80, 29.33, 28.84.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₁₇H₂₅NO₅Na: 346.1625; found: 346.1618.

(*S*)-2-((*tert*-Butoxycarbonyl)amino)-2-(2-fluorophenyl)acetic Acid (6)⁸

From *tert*-butyl (2-(2-fluorophenyl)acetoxy)carbamate (53.8 mg, 0.2 mmol) using (*R*,*R*)-**FeBIPF**₂ (2 mol%) and TMP (0.2 mmol, 34 μ L) at -30 °C for 16 h. Flash column chromatography on silica gel with *n*-hexane/EtOAc (5:1, plus 0.2% HOAc) as the eluent provided **6** as a colorless gum (50.9 mg, 95% yield, 90% ee).

HPLC analysis for determining the ee value: Daicel Chiralpak IG column, 250 × 4.6 mm, mobile phase *n*-hexane/*i*PrOH = 9:1 (v/v) with 0.1% TFA, flow rate 1.0 mL/min, UV detection at 210 nm, 25 °C; t_1 = 14.5 min, t_2 = 24.0 min.

 $[\alpha]_{D}^{25}$ +109.4 (*c* 1.0, MeOH).

¹H NMR (300 MHz, CD₃OD): δ = 7.36 (dt, *J* = 18.9, 7.6 Hz, 2 H), 7.13 (dt, *J* = 18.2, 8.4 Hz, 2 H), 5.50 (s, 1 H), 1.43 (s, 9 H).

¹³C NMR (75 MHz, CD₃OD): δ = 173.59, 163.00 (d, J = 245.25 Hz), 157.56, 131.31 (d, J = 8.25 Hz), 130.45, 126.50 (d, J = 15.00 Hz), 125.65 (d, J = 3.75 Hz), 116.66 (d, J = 21.75 Hz), 81.05, 53.03, 28.80.

¹⁹F NMR (282 MHz, CD₃OD): δ = -119.58.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₁₃H₁₆FNO₄Na: 292.0956; found: 292.0946.

(S)-2-((tert-Butoxycarbonyl)amino)-2-(2-chlorophenyl)acetic Acid $(7)^{\rm 9}$

From *tert*-butyl (2-(2-chlorophenyl)acetoxy)carbamate (57.1 mg, 0.2 mmol) using (*R*,*R*)-**FeBIPF**₂ (2 mol%) and TMP (0.2 mmol, 34 μ L) at – 30 °C for 16 h. Flash column chromatography on silica gel with *n*-hexane/EtOAc (5:1, plus 0.2% HOAc) as the eluent provided **7** as a colorless gum (48.8 mg, 85% yield, 88% ee).

HPLC analysis for determining the ee value: Daicel Chiralpak IG column, 250 × 4.6 mm, mobile phase *n*-hexane/*i*PrOH = 9:1 (v/v) with 0.1% TFA, flow rate 1.0 mL/min, UV detection at 210 nm, 25 °C; t_1 = 15.1 min, t_2 = 24.5 min.

 $[\alpha]_{D}^{25}$ +94.4 (*c* 1.0, MeOH).

¹H NMR (300 MHz, CD₃OD): δ = 7.41 (q, *J* = 4.0 Hz, 2 H), 7.35–7.20 (m, 2 H), 5.67 (s, 1 H), 1.43 (s, 9 H).

¹³C NMR (75 MHz, CD₃OD): δ = 173.71, 157.56, 136.93, 135.18, 130.94, 130.78, 130.39, 128.47, 81.02, 56.39, 28.81.

HRMS (ESI): $m/z [M + Na]^+$ calcd for $C_{13}H_{16}CINO_4Na$: 308.0660; found: 308.0650.

(S)-2-((*tert*-Butoxycarbonyl)amino)-2-(2,4-difluorophenyl)acetic Acid (8)

From *tert*-butyl (2-(2,4-difluorophenyl)acetoxy)carbamate (57.5 mg, 0.2 mmol) using (*R*,*R*)-**FeBIPF**₂ (2 mol%) and TMP (0.2 mmol, 34 μ L) at -30 °C for 16 h. Flash column chromatography on silica gel with *n*-hexane/EtOAc (5:1, plus 0.2% HOAc) as the eluent provided **8** as a colorless gum (52.6 mg, 91% yield, 90% ee).

HPLC analysis for determining the ee value: Daicel Chiralpak IG column, 250 × 4.6 mm, mobile phase *n*-hexane/iPrOH = 9:1 (v/v) with 0.1% TFA, flow rate 1.0 mL/min, UV detection at 210 nm, 25 °C; t_1 = 10.1 min, t_2 = 16.6 min.

[α]_D²⁵ +116.2 (*c* 1.0, MeOH).

¹H NMR (300 MHz, CD₃OD): δ = 7.42 (td, *J* = 8.7, 6.3 Hz, 1 H), 7.07–6.84 (m, 2 H), 5.47 (s, 1 H), 1.43 (s, 9 H).

¹³C NMR (75 MHz, CD₃OD): δ = 173.33, 164.35 (dd, *J* = 246.75, 12.00 Hz), 162.19 (dd, *J* = 247.50, 12.00 Hz), 157.52, 131.63, 123.09, 112.62 (dd, *J* = 21.00, 3.75 Hz), 104.92 (t, *J* = 26.25 Hz), 81.11, 52.64, 28.79.

 ^{19}F NMR (282 MHz, CD₃OD): δ = –112.07 (d, J = 7.7 Hz), –114.99 (d, J = 7.7 Hz).

HRMS (ESI): $m/z [M + Na]^+$ calcd for $C_{13}H_{15}F_2NO_4Na$: 310.0861; found: 310.0853.





THIEME OPEN

(S)-2-((*tert*-Butoxycarbonyl)amino)-2-(2,6-dichlorophenyl)acetic Acid (9)

From *tert*-butyl (2-(2,6-dichlorophenyl)acetoxy)carbamate (64.0 mg, 0.2 mmol) using (*R*,*R*)-**FeBIPF**₂ (2 mol%) and TMP (0.2 mmol, 34 μ L) at -30 °C for 16 h. Flash column chromatography on silica gel with *n*-hexane/EtOAc (5:1, plus 0.2% HOAc) as the eluent provided **9** as a colorless gum (53.6 mg, 84% yield, 91% ee).

HPLC analysis for determining the ee value: Daicel Chiralpak IG column, 250 × 4.6 mm, mobile phase *n*-hexane/*i*PrOH = 9:1 (v/v) with 0.1% TFA, flow rate 1.0 mL/min, UV detection at 210 nm, 25 °C; t_1 = 11.8 min, t_2 = 21.1 min.

 $[\alpha]_{D}^{25}$ +104.7 (*c* 1.0, MeOH).

¹H NMR (300 MHz, CD₃OD): δ = 7.39 (d, *J* = 7.4 Hz, 2 H), 7.28 (dd, *J* = 8.9, 7.1 Hz, 1 H), 6.16 (d, *J* = 41.5 Hz, 1 H), 1.44 (s, 9 H).

 ^{13}C NMR (75 MHz, CD₃OD): δ = 172.66, 157.36, 136.89, 135.74, 131.24, 130.08, 81.32, 55.18, 28.76.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₁₃H₁₅Cl₂NO₄Na: 342.0270; found: 342.0264.

(S)-2-(3,5-Bis(trifluoromethyl)phenyl)-2-((*tert*-butoxycarbonyl)amino)acetic Acid (10)

From *tert*-butyl (2-(3,5-bis(trifluoromethyl)phenyl)acetoxy)carbamate (77.5 mg, 0.2 mmol) using (*R*,*R*)-**FeBIPF**₂ (2 mol%) and TMP (0.2 mmol, 34 μ L) at -30 °C for 16 h. Flash column chromatography on silica gel with *n*-hexane/EtOAc (5:1, plus 0.2% HOAc) as the eluent provided **10** as a colorless gum (62.4 mg, 81% yield, 96% ee).

HPLC analysis for determining the ee value: Daicel Chiralpak IG column, 250 × 4.6 mm, mobile phase *n*-hexane/*i*PrOH = 19:1 (v/v) with 0.1% TFA, flow rate 1.0 mL/min, UV detection at 210 nm, 25 °C; t_1 = 4.7 min, t_2 = 5.3 min.

[α]_D²⁵ +105.8 (*c* 1.0, MeOH).

¹H NMR (300 MHz, CD₃OD): δ = 8.03 (d, *J* = 1.7 Hz, 2 H), 7.92 (s, 1 H), 5.45 (s, 1 H), 1.44 (s, 9 H).

¹³C NMR (75 MHz, CD₃OD): δ = 172.44, 157.53, 142.95, 133.05 (q, *J* = 33.00 Hz), 129.32, 124.89 (q, *J* = 270.00 Hz), 122.91 (q, *J* = 3.75 Hz), 81.38, 58.49, 28.74.

¹⁹F NMR (282 MHz, CD_3OD): $\delta = -64.37$.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₁₅H₁₅F₆NO₄Na: 410.0797; found: 410.0788.

(S)-2-((*tert*-Butoxycarbonyl)amino)-2-(3,5-dimethoxyphenyl)acetic Acid (11)¹⁰

From *tert*-butyl (2-(3,5-dimethoxyphenyl)acetoxy)carbamate (62.3 mg, 0.2 mmol) using (*R*,*R*)-**FeBIPF**₂ (2 mol%) and TMP (0.2 mmol, 34 μ L) at -30 °C for 16 h. Flash column chromatography on silica gel with *n*-hexane/EtOAc (6:1, plus 0.2% HOAc) as the eluent provided **11** as a colorless gum (58.3 mg, 94% yield, 94% ee).

HPLC analysis for determining the ee value: Daicel Chiralpak IG column, 250 × 4.6 mm, mobile phase *n*-hexane/iPrOH = 9:1 (v/v) with 0.1% TFA, flow rate 1.0 mL/min, UV detection at 210 nm, 25 °C; t_1 = 21.5 min, t_2 = 29.4 min.

 $[\alpha]_{D}^{25}$ +126.9 (*c* 1.0, MeOH).

¹H NMR (300 MHz, CD₃OD): δ = 6.61–6.36 (m, 3 H), 5.11 (s, 1 H), 3.73 (s, 6 H), 1.44 (s, 9 H).

¹³C NMR (75 MHz, CD₃OD): δ = 174.19, 162.60, 157.57, 140.83, 106.69, 101.28, 80.98, 59.35, 55.95, 28.83.

HRMS (ESI): $m/z \,[M + Na]^*$ cacld. for $C_{15}H_{21}NO_6Na$: 334.1261; found: 334.1251.

(S)-2-((tert-Butoxycarbonyl)amino)-2-phenylpropanoic Acid (12)

From *tert*-butyl ((2-phenylpropanoyl)oxy)carbamate⁵ (53.1 mg, 0.2 mmol) using (*R*,*R*)-**FeBIPF**₂ (5 mol%) and TMP (0.4 mmol, 68 μ L) at –50 °C for 40 h. Flash column chromatography on silica gel with *n*-hexane/EtOAc (6:1, plus 0.2% HOAc) as the eluent provided **12** as a colorless gum (48.2 mg, 91% yield, 96% ee).

HPLC analysis for determining the ee value: Daicel Chiralpak IG column, 250 × 4.6 mm, mobile phase *n*-hexane/iPrOH = 9:1 (v/v) with 0.1% TFA, flow rate 1.0 mL/min, UV detection at 210 nm, 25 °C; t_1 = 8.0 min, t_2 = 13.0 min.

 $[\alpha]_{D}^{25}$ +61.5 (*c* 1.0, MeOH).

Analytical data are consistent with a recent report.⁵

(S)-2-((*tert*-Butoxycarbonyl)amino)-2-(*p*-tolyl)propanoic Acid (13) From *tert*-butyl ((2-(*p*-tolyl)propanoyl)oxy)carbamate⁵ (55.9 mg, 0.2 mmol) using (*R*,*R*)-**FeBIPF**₂ (5 mol%) and TMP (0.2 mmol, 34 μ L) at

-30 °C for 40 h. Flash column chromatography on silica gel with *n*-hexane/EtOAc (6:1, plus 0.2% HOAc) as the eluent provided **13** as a colorless gum (48.8 mg, 87% yield, 90% ee).

HPLC analysis for determining the ee value: Daicel Chiralpak IG column, 250 × 4.6 mm, mobile phase *n*-hexane/iPrOH = 9:1 (v/v) with 0.1% TFA, flow rate 1.0 mL/min, UV detection at 210 nm, 25 °C; t_1 = 7.9 min, t_2 = 11.7 min.

 $[\alpha]_{D}^{25}$ +52.0 (*c* 1.0, MeOH).

Analytical data are consistent with a recent report.⁵

(S)-2-((*tert*-Butoxycarbonyl)amino)-2-(4-(*tert*-butyl)phenyl)propanoic Acid (14)

From *tert*-butyl ((2-(4-(*tert*-butyl)phenyl)propanoyl)oxy)carbamate⁵ (64.3 mg, 0.2 mmol) using (*R*,*R*)-**FeBIPF**₂ (5 mol%) and TMP (0.2 mmol, 34 μ L). Flash column chromatography on silica gel with *n*-hexane/EtOAc (6:1, plus 0.2% HOAc) as the eluent provided **14** as a colorless gum (57.9 mg, 90% yield, 93% ee).

HPLC analysis for determining the ee value: Daicel Chiralpak IG column, 250 × 4.6 mm, mobile phase *n*-hexane/*i*PrOH = 9:1 (v/v) with 0.1% TFA, flow rate 1.0 mL/min, UV detection at 210 nm, 25 °C; t_1 = 5.8 min, t_2 = 8.1 min.

 $[\alpha]_{D}^{25}$ +48.3 (*c* 1.0, MeOH).

Analytical data are consistent with a recent report.⁵

(S)-2-([1,1'-Biphenyl]-4-yl)-2-((*tert*-butoxycarbonyl)amino)propanoic Acid (15)

From *tert*-butyl ((2-([1,1'-biphenyl]-4-yl)propanoyl)oxy)carbamate (68.3 mg, 0.2 mmol) using (*R*,*R*)-**FeBIPF2** (5 mol%) and TMP (0.2 mmol, 34 μ L). Flash column chromatography on silica gel with *n*-hexane/EtOAc (6:1, plus 0.2% HOAc) as the eluent provided **15** as a colorless gum (57.9 mg, 85% yield, 94% ee).

HPLC analysis for determining the ee value: Daicel Chiralpak IG column, 250 × 4.6 mm, mobile phase *n*-hexane/iPrOH = 9:1 (v/v) with 0.1% TFA, flow rate 1.0 mL/min, UV detection at 210 nm, 25 °C; t_1 = 10.7 min, t_2 = 17.7 min.

[α]_D²⁵ +52.6 (*c* 1.0, MeOH).

¹H NMR (300 MHz, CD₃OD): δ = 7.60 (d, *J* = 8.8 Hz, 6 H), 7.41 (q, *J* = 6.0, 4.7 Hz, 2 H), 7.36–7.26 (m, 1 H), 1.94 (s, 3 H), 1.39 (s, 9 H).

		THIEME	
Synthesis	K. Yin, E. Meggers	OPEN ACCESS	

2678

 ^{13}C NMR (75 MHz, CD₃OD): δ = 176.13, 156.62, 141.81, 141.68, 129.84, 128.42, 127.93, 127.80, 127.69, 62.70, 28.66, 24.18.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₂₀H₂₃NO₄Na: 364.1519; found: 364.1512.

(S)-2-((*tert*-Butoxycarbonyl)amino)-2-(4-chlorophenyl)propanoic Acid (16)

From *tert*-butyl ((2-(4-chlorophenyl)propanoyl)oxy)carbamate⁵ (60.0 mg, 0.2 mmol) using (*R*,*R*)-**FeBIPF**₂ (5 mol%) and TMP (0.2 mmol, 34 μ L). Flash column chromatography on silica gel with *n*-hexane/EtOAc (6:1, plus 0.2% HOAc) as the eluent provided **16** as a colorless gum (54.3 mg, 91% yield, 93% ee).

HPLC analysis for determining the ee value: Daicel Chiralpak IG column, 250 × 4.6 mm, mobile phase *n*-hexane/iPrOH = 9:1 (v/v) with 0.1% TFA, flow rate 1.0 mL/min, UV detection at 210 nm, 25 °C; t_1 = 6.5 min, t_2 = 7.7 min.

[α]_D²⁵ +51.0 (*c* 1.0, MeOH).

Analytical data are consistent with a recent report.⁵

(S)-2-(3-Benzoylphenyl)-2-((*tert*-butoxycarbonyl)amino)propanoic Acid (17)

From *tert*-butyl ((2-(3-benzoylphenyl)propanoyl)oxy)carbamate (73.9 mg, 0.2 mmol) using (*R*,*R*)-**FeBIPF**₂ (5 mol%) and TMP (0.2 mmol, 34 μ L). Flash column chromatography on silica gel with *n*-hexane/EtOAc (6/1, plus 0.2% HOAc) as the eluent provided **17** as a colorless gum (67.7 mg, 91% yield, 96%ee).

HPLC analysis for determining the ee value: Daicel Chiralpak IG column, 250 × 4.6 mm, mobile phase *n*-hexane/iPrOH = 9/1 (v/v) with 0.1% TFA, flow rate 1.0 mL/min, UV detection at 210 nm, 25 °C; t_1 = 27.0 min, t_2 = 34.2 min. [α]_D²⁵ = +31.0° (*c* 1.0, MeOH). Analytical data are consistent with a recent report.⁶

(S)-2-(Benzo[d][1,3]dioxol-5-yl)-2-((*tert*-butoxycarbonyl)amino)propanoic Acid (18)

From *tert*-butyl ((2-(benzo[*d*][1,3]dioxol-5-yl)propanoyl)oxy)carbamate (61.9 mg, 0.2 mmol) using (*R*,*R*)-**FeBIPF**₂ (5 mol%) and TMP (0.2 mmol, 34 μ L). Flash column chromatography on silica gel with *n*-hexane/EtOAc (6:1, plus 0.2% HOAc) as the eluent provided **18** as a colorless gum (55.7 mg, 90% yield, 80% ee).

HPLC analysis for determining the ee value: Daicel Chiralpak IG column, 250 × 4.6 mm, mobile phase *n*-hexane/iPrOH = 9:1 (v/v) with 0.1% TFA, flow rate 1.0 mL/min, UV detection at 210 nm, 25 °C; t_1 = 12.6 min, t_2 = 16.5 min.

 $[\alpha]_{D}^{25}$ +59.2 (*c* 1.0, MeOH).

¹H NMR (300 MHz, CD₃OD): δ = 6.97 (d, J = 7.5 Hz, 2 H), 6.77 (d, J = 8.1 Hz, 1 H), 5.93 (s, 2 H), 1.88 (s, 3 H), 1.40 (s, 9 H).

¹³C NMR (75 MHz, CD₃OD): δ = 176.17, 156.53, 149.15, 148.44, 136.62, 120.60, 108.67, 107.91, 102.51, 82.50, 62.54, 28.65, 24.06.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₁₅H₁₉NO₆Na: 332.1105; found: 332.1100.

(S)-2-((*tert*-Butoxycarbonyl)amino)-2-(naphthalen-2-yl)propanoic Acid (19)

From *tert*-butyl ((2-(naphthalen-2-yl)propanoyl)oxy)carbamate (63.1 mg, 0.2 mmol) using (*R*,*R*)-**FeBIPF**₂ (5 mol%) and TMP (0.2 mmol, 34 μ L) at –30 °C for 40 h. Flash column chromatography on silica gel with *n*-hexane/EtOAc (6:1, plus 0.2% HOAc) as the eluent provided **19** as a colorless gum (57.2 mg, 91% yield, 91% ee).

HPLC analysis for determining the ee value: Daicel Chiralpak IG column, 250 × 4.6 mm, mobile phase *n*-hexane/iPrOH = 9:1 (v/v) with 0.1% TFA, flow rate 1.0 mL/min, UV detection at 210 nm, 25 °C; t_1 = 10.5 min, t_2 = 12.8 min.

 $[\alpha]_{D}^{25}$ +53.1 (*c* 1.0, MeOH).

Analytical data are consistent with a recent report.⁶

(S)-2-((*tert*-Butoxycarbonyl)amino)-2-(naphthalen-1-yl)propanoic Acid (20)

From *tert*-butyl ((2-(naphthalen-1-yl)propanoyl)oxy)carbamate (63.1 mg, 0.2 mmol) using (*R*,*R*)-**FeBIPF**₂ (5 mol%) and TMP (0.2 mmol, 34 μ L) at –30 °C for 40 h. Flash column chromatography on silica gel with *n*-hexane/EtOAc (6:1, plus 0.2% HOAc) as the eluent provided **20** as a colorless gum (53.2 mg, 84% yield, 93% ee).

HPLC analysis for determining the ee value: Daicel Chiralpak IG column, 250 × 4.6 mm, mobile phase *n*-hexane/iPrOH = 9:1 (v/v) with 0.1% TFA, flow rate 1.0 mL/min, UV detection at 210 nm, 25 °C; t_1 = 14.8 min, t_2 = 19.2 min.

 $[\alpha]_{D}^{25}$ +52.6 (*c* 1.0, MeOH).

¹H NMR (300 MHz, CD₃OD): δ = 8.20 (dd, *J* = 6.6, 3.4 Hz, 1 H), 7.94–7.80 (m, 2 H), 7.74 (d, *J* = 7.4 Hz, 1 H), 7.54–7.35 (m, 3 H), 2.17 (s, 3 H), 1.07 (d, *J* = 103.7 Hz, 9 H).

 ^{13}C NMR (75 MHz, CD₃OD): δ = 177.29, 153.79, 137.54, 135.82, 132.15, 130.12, 129.81, 127.10, 126.84, 126.22, 125.88, 125.47, 81.14, 62.53, 28.36, 25.74.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₁₈H₂₁NO₄Na: 338.1363; found: 338.1360.

(S)-2-((*tert*-Butoxycarbonyl)amino)-2-(thiophen-3-yl)propanoic Acid (21)

From *tert*-butyl ((2-(thiophen-3-yl)propanoyl)oxy)carbamate (54.3 mg, 0.2 mmol) using (*R*,*R*)-**FeBIPF**₂ (5 mol%) and TMP (0.2 mmol, 34 μ L) at -30 °C for 40 h. Flash column chromatography on silica gel with *n*-hexane/EtOAc (6:1, plus 0.2% HOAc) as the eluent provided **21** as a colorless gum (46.3 mg, 85% yield, 88% ee).

HPLC analysis for determining the ee value: Daicel Chiralpak IG column, 250 × 4.6 mm, mobile phase *n*-hexane/iPrOH = 9:1 (v/v) with 0.1% TFA, flow rate 1.0 mL/min, UV detection at 210 nm, 25 °C; t_1 = 9.3 min, t_2 = 15.0 min.

 $[\alpha]_{D}^{25}$ +31.6 (*c* 1.0, MeOH).

Analytical data are consistent with a recent report.⁶

(S)-2-((*tert*-Butoxycarbonyl)amino)-2-cyclopentyl-2-phenylacetic Acid (22)

From *tert*-butyl (2-cyclopentyl-2-phenylacetoxy)carbamate (63.9 mg, 0.2 mmol) using (*R*,*R*)-**FeBIPF**₂ (5 mol%) and TMP (0.2 mmol, 34 μ L) at -30 °C for 40 h. Flash column chromatography on silica gel with *n*-hexane/EtOAc (9:1, plus 0.2% HOAc) as the eluent provided **22** as a colorless gum (51.9 mg, 81% yield, 96% ee).

HPLC analysis for determining the ee value: Daicel Chiralpak IG column, 250 × 4.6 mm, mobile phase *n*-hexane/*i*PrOH = 4:1 (v/v) with 0.1% TFA, flow rate 1.0 mL/min, UV detection at 210 nm, 25 °C; t_1 = 5.3 min, t_2 = 27.1 min.

 $[\alpha]_{D}^{25}$ +29.4 (*c* 1.0, MeOH).

¹H NMR (300 MHz, CD₃OD): δ = 7.58 (d, *J* = 7.6 Hz, 2 H), 7.30 (dt, *J* = 14.6, 7.1 Hz, 3 H), 2.90 (s, 1 H), 1.67 (s, 2 H), 1.61–1.30 (m, 12 H), 1.17 (s, 2 H).

		2679
Synthesis	K. Yin, E. Meggers	THIEME OPEN ACCESS

¹³C NMR (75 MHz, CD₃OD): δ = 175.71, 157.11, 141.45, 128.82, 128.32, 128.08, 80.75, 68.52, 29.00, 28.76, 26.24, 26.11.

HRMS (ESI): $m/z [M + Na]^*$ calcd for $C_{18}H_{25}NO_4Na$: 342.1676; found: 342.1670.

(S)-2-((*tert*-Butoxycarbonyl)amino)-2-cyclohexyl-2-phenylacetic Acid (23)

From *tert*-butyl (2-cyclohexyl-2-phenylacetoxy)carbamate (66.7 mg, 0.2 mmol) using (*R*,*R*)-**FeBIPF**₂ (5 mol%) and TMP (0.4 mmol, 68 μ L) at –50 °C for 40 h. Flash column chromatography on silica gel with *n*-hexane/EtOAc (9:1, plus 0.2% HOAc) as the eluent provided **23** as a colorless gum (62.1 mg, 93% yield, 98% ee).

HPLC analysis for determining the ee value: Daicel Chiralpak IG column, 250 × 4.6 mm, mobile phase *n*-hexane/*i*PrOH = 4:1 (v/v) with 0.1% TFA, flow rate 1.0 mL/min, UV detection at 210 nm, 25 °C; t_1 = 6.0 min, t_2 = 26.0 min.

 $[\alpha]_{D}^{25}$ +29.0 (*c* 1.0, MeOH).

Analytical data are consistent with a recent report.⁶

(S)-1-((*tert*-Butoxycarbonyl)amino)-1,2,3,4-tetrahydronaphthalene-1-carboxylic Acid (24)

From *tert*-butyl ((1,2,3,4-tetrahydronaphthalene-1-carbonyl)oxy)carbamate (58.3 mg, 0.2 mmol) using (*R*,*R*)-**FeBIPF**₂ (5 mol%) and TMP (0.2 mmol, 34 μ L) at -30 °C for 40 h. Flash column chromatography on silica gel with *n*-hexane/EtOAc (8:1, plus 0.2% HOAc) as the eluent provided **24** as a colorless gum (50.3 mg, 86% yield, 78% ee).

HPLC analysis for determining the ee value: Daicel Chiralpak IG column, 250 × 4.6 mm, mobile phase *n*-hexane/iPrOH = 9:1 (v/v) with 0.1% TFA, flow rate 1.0 mL/min, UV detection at 210 nm, 25 °C; t_1 = 8.9 min, t_2 = 11.3 min.

 $[\alpha]_{D}^{25}$ +88.2 (*c* 1.0, MeOH).

¹H NMR (300 MHz, CD₃OD): δ = 7.45 (d, J = 7.4 Hz, 1 H), 7.15 (tdd, J = 12.0, 7.0, 2.0 Hz, 3 H), 2.92–2.71 (m, 2 H), 2.51 (s, 1 H), 2.43–2.28 (m, 1 H), 2.05 (s, 1 H), 1.87 (p, J = 6.2 Hz, 1 H), 1.41 (s, 9 H).

 ^{13}C NMR (75 MHz, CD₃OD): δ = 176.55, 139.63, 130.38, 128.82, 128.16, 128.14, 127.29, 80.31, 61.79, 32.62, 30.47, 28.70, 20.68.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₁₆H₂₁NO₄Na: 314.1363; found: 314.1357.

Conflict of Interest

The authors declare no conflict of interest.

Funding Information

This project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement No 883212).

Supporting Information

Synthesis of catalysts, NMR spectra, and HPLC traces. Supporting information for this article is available online at https://doi.org/10.1055/s-0043-1775371.

References

- (1) Reviews on applications of unnatural and non-proteinogenic α amino acids: (a) Dougherty, D. A. Curr. Opin. Chem. Biol. 2000, 4, 645. (b) Hodgson, D. R. W.; Sanderson, J. M. Chem. Soc. Rev. 2004, 33, 422. (c) Bhonsle, J. B.; Clark, T.; Bartolotti, L.; Hicks, R. P. Curr. Top. Med. Chem. 2013, 13, 3205. (d) Stevenazzi, A.; Marchini, M.; Sandrone, G.; Vergani, B.; Lattanzio, M. Bioorg. Med. Chem. Lett. 2014, 24, 5349. (e) Blaskovich, M. A. T. J. Med. Chem. 2016, 59, 10807. (f) Agostini, F.; Völler, J.-S.; Koksch, B.; Acevedo-Rocha, C. G.; Kubyshkin, V.; Budisa, N. Angew. Chem. Int. Ed. 2017, 56, 9680. (g) Henninot, A.; Collins, J. C.; Nuss, J. M. J. Med. Chem. 2018, 61, 1382. (h) Narancic, T.; Almahboub, S. A.; O'Connor, K. E. World J. Microbiol. Biotechnol. 2019, 35, 67. (i) Cheng, Z.; Kuru, E.; Sachdeva, A.; Vendrell, M. Nat. Rev. Chem. 2020, 4, 275. (j) Mei, H.; Han, J.; White, S.; Graham, D. J.; Izawa, K.; Sato, T.; Fustero, S.; Meanwell, N. A.; Soloshonok, V. A. Chem. Eur. J. 2020, 26, 11349. (k) Yokoo, H.; Hirano, M.; Misawa, T.; Demizu, Y. ChemMedChem 2021, 16, 1226.
- (2) Reviews on the synthesis of α -amino acids: (a) Williams, R. M.; Hendrix, J. A. Chem. Rev. 1992, 92, 889. (b) Ma, J.-A. Angew. Chem. Int. Ed. 2003, 42, 4290. (c) Maruoka, K. Proc. Jpn. Acad., Ser. B 2003, 79, 181. (d) Breuer, M.; Ditrich, K.; Habicher, T.; Hauer, B.; Keßeler, M.; Stürmer, R.; Zelinski, T. Angew. Chem. Int. Ed. 2004, 43, 788. (e) Nájera, C.; Sansano, J. M. Chem. Rev. 2007, 107, 4584. (f) Kim, Y.; Park, J.; Kim, M.-J. ChemCatChem 2011, 3, 271. (g) Smith, A. M. R.; Hii, K. K. Chem. Rev. 2011, 111, 1637. (h) So, S. M.; Kim, H.; Mui, L.; Chin, J. Eur. J. Org. Chem. 2012, 229. (i) D'Arrigo, P.; Cerioli, L.; Servi, S.; Viani, F.; Tessaro, D. Catal. Sci. Technol. 2012, 2, 1606. (j) Bera, K.; Namboothiri, I. N. N. Asian J. Org. Chem. 2014, 3, 1234. (k) Metz, A. E.; Kozlowski, M. C. J. Org. Chem. 2015, 80, 1. (1) He, G.; Wang, B.; Nack, W. A.; Chen, G. Acc. Chem. Res. 2016, 49, 635. (m) Xue, Y.-P.; Cao, C.-H.; Zheng, Y.-G. Chem. Soc. Rev. 2018, 47, 1516. (n) Moschner, J.; Stulberg, V.; Fernandes, R.; Huhmann, S.; Leppkes, J.; Koksch, B. Chem. Rev. 2019, 119, 10718. (o) Larionov, V. A.; Stoletova, N. V.; Maleev, V. I. Adv. Synth. Catal. 2020, 362, 4325. (p) Ponra, S.; Boudet, B.; Phansavath, P.; Ratovelomanana-Vidal, V. Synthesis 2021, 53, 193. (q) Lin, K.; Shi, A.; Shi, C.; Lin, J.; Lin, H. Front. Chem. 2021, 9, 687817.
- (3) For recent examples on the asymmetric synthesis of α-amino acids, see: (a) Kang, Q.-K.; Selvakumar, S.; Maruoka, K. Org. Lett. **2019**, *21*, 2294. (b) Bendelsmith, A. J.; Kim, S. C.; Wasa, M.; Roche, S. P.; Jacobsen, E. N. J. Am. Chem. Soc. **2019**, *141*, 11414. (c) Han, J.; Romoff, T. T.; Moriwaki, H.; Konno, H.; Soloshonok, V. A. ACS Omega **2019**, *4*, 18942. (d) Zou, Y.; Han, J.; Saghyan, A. S.; Mkrtchyan, A. F.; Konno, H.; Moriwaki, H.; Izawa, K.; Soloshonok, V. A. Molecules **2020**, *25*, 2739. (e) Yang, Z.-P.; Freas, D. J.; Fu, G. C. J. Am. Chem. Soc. **2021**, *143*, 8614. (f) Shatskiy, A.; Axelsson, A.; Stepanova, E. V.; Liu, J.-Q.; Temerdashev, A. Z.; Kore, B. P.; Blomkvist, B.; Gardner, J. M.; Dinér, P.; Kärkäs, M. D. Chem. Sci. **2021**, *12*, 5430.
- (4) Ye, C.-X.; Shen, X.; Chen, S.; Meggers, E. Nat. Chem. 2022, 14, 566.
- (5) Zhou, B.; Ye, C.-X.; Meggers, E. Eur. J. Org. Chem. 2023, e202300296.
- (6) See also: Ye, C.-X.; Dansby, D. R.; Chen, S.; Meggers, E. Nat. Synth. 2023, 2, 645.
- (7) For a recent review on metal-catalyzed enantioconvergent transformations, see: Yus, M.; Nájera, C.; Foubelo, F.; Sansano, J. M. Chem. Rev. 2023, 123, 11817.

2680 THIEME

OPEN ACCESS

Syn <mark>thesis</mark>	K. Yin, E. Meggers

- (8) Arosio, D.; Caligiuri, A.; D'Arrigo, P.; Pedrocchi-Fantoni, G.; Rossi, C.; Saraceno, C.; Servi, S.; Tessaro, D. Adv. Synth. Catal. 2007, 349, 1345.
- (9) Ferraboschi, P.; Mieri, M. D.; Galimberti, F. Tetrahedron: Asymmetry **2010**, *21*, 2136.
- (10) Evans, D. A.; Dinsmore, C. J.; Evrard, D. A.; DeVries, K. M. J. Am. Chem. Soc. **1993**, *115*, 6426.