SUPPORTING INFORMATION

Quaternary $\beta_2^2$-Amino Acid Derivatives by Asymmetric Addition of Isoxazolidin-5-ones to para-Quinone Methides

Andreas Eitzinger, Michael Winter, Johannes Schörgenhumer, and Mario Waser*

e-mail: mario.waser@jku.at

Johannes Kepler University Linz, Institute of Organic Chemistry, Altenbergerstraße 69, 4040 Linz, Austria, Fax: +43 732 2468 8747; Tel: +43 732 2468 8748

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1. General Information:

1.1. General Methods

$^1$H- and $^{13}$C-NMR spectra were recorded on a Bruker Avance III 300 MHz spectrometer with a broad band observe probe and a sample changer for 16 samples, on a Bruker Avance DRX 500 MHz spectrometer, and on a Bruker Avance III 700 MHz spectrometer with an Ascend magnet and TCI cryoprobe, which are both property of the Austro-Czech NMR-Research Center “RERI-uasb”. All NMR spectra were referenced on the solvent peak and chemical shifts are given in ppm.

High resolution mass spectra were obtained using an Agilent 6520 Q-TOF mass spectrometer with an ESI source and an Agilent G1607A coaxial sprayer or a Thermo Fisher Scientific LTQ Orbitrap XL with an Ion Max API Source. Analyses were made in the positive ionization mode if not otherwise stated. Purine (exact mass for [M+H]$^+$ = 121.050873) and 1,2,3,4,5,6-hexakis(2,2,3,3-tetrafluoropropoxy)-1,3,5,2,4,6-triazatriphosphinane (exact mass for [M+H]$^+$ = 922.009798) were used for internal mass calibration.

HPLC was performed using a Thermo Scientific Dionex Ultimate 3000 system with diode array detector with a CHIRAL ART Cellulose-SB or Amylose-SA (250 x 4.6 mm, 5 µm) chiral stationary phase. Semi-preparative HPLC was performed on a Thermo Scientific Dionex Ultimate 3000 system with a variable wavelength detector and a normal phase silica column (5 µm particle size, L x I.D. = 250 x 10 mm).

Optical rotations were recorded on a Schmidt + Haensch Polarimeter Model UniPol L1000.

All chemicals were purchased from commercial suppliers and used without further purification unless otherwise stated. K$_2$CO$_3$ and Cs$_2$CO$_3$ were flame-dried in vacuo prior to use. Dry solvents were obtained from an MBraun-SPS-800 solvent purification system. All reactions were carried out under argon atmosphere.

Meldrums acid derivatives$^1$ 9, (toluylsulfonyl)methyl N-hydroxycarbamates$^2$ 10 and para-quinone methides$^3$ 2 were prepared by reported procedures.

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1.2. Single-Crystal Analysis

Single-crystal structure analyses were carried out on a Bruker D8 Quest Eco diffractometer operating with Mo-K\(_\alpha\) radiation (\(\lambda = 0.71073\) Å). Further crystallographic and refinement data can be found in Table S1. The structures were solved by direct methods (SHELXS-97)\(^4\) and refined by full-matrix least squares on \(F^2\) (SHELXL-97).\(^5\) The H atoms were calculated geometrically, and a riding model was applied in the refinement process. CCDC 1911984 and 1943927 contain the supplementary crystallographic data for compounds 3j and 3b. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre at www.ccdc.cam.ac.uk.

<table>
<thead>
<tr>
<th>Table 1: Crystal Data, Data Collection and Structure Refinement Details for Compound 3j</th>
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<td><strong>Crystal Data</strong></td>
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<td>Formula weight [g/mol]</td>
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<tr>
<td>Color</td>
</tr>
<tr>
<td>Crystal size [mm]</td>
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<tr>
<td>Space group</td>
</tr>
<tr>
<td>(a) [Å]</td>
</tr>
<tr>
<td>(b) [Å]</td>
</tr>
<tr>
<td>(c) [Å]</td>
</tr>
<tr>
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<tr>
<td>(\beta) [°]</td>
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<tr>
<td>(\gamma) [°]</td>
</tr>
<tr>
<td>(V) [Å(^3)]</td>
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<tr>
<td>(Z)</td>
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<td>(D_{\text{calc}}) [g/cm(^3)]</td>
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<tr>
<td>(\mu) [mm(^{-1})]</td>
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<tr>
<td>(T) [K]</td>
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<tr>
<td>(\Delta\rho_{\text{min}}, \Delta\rho_{\text{max}}) [e Å(^{-3})]</td>
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<tr>
<td>(F(000))</td>
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<tr>
<td>(R_{\text{int}})</td>
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$R_t (R[F^2 \geq 2\sigma(F^2)])$ 0.065
\n$wR_2 (wR(F^2))$ 0.123
\nGooF 1.07
\nFlack x 0.092(7)
\nCCDC no. 1911984

Figure 1: Crystal Structure of 3j

Table 2: Crystal Data, Data Collection and Structure Refinement Details for Compound 3b

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<td>$b$ [Å]</td>
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<td>$c$ [Å]</td>
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<td>$\alpha$ [°]</td>
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<td>$\beta$ [°]</td>
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Figure 2: Crystal Structure of 3b
2. Further Catalyst Screening

2.1 Screening of Other Chiral Ammonium Salt Catalysts

Table 3: Further Catalyst Screening: All reactions were run at room temperature using 0.1 mmol 1a and 0.15 mmol 2a (0.1 M with respect to 1a); [a] Isolated Yields; [b] Determined by crude product NMR; [c] Determined by HPLC using a chiral stationary phase

<table>
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<tr>
<th>Entry</th>
<th>Catalyst (mol%)</th>
<th>Solvent</th>
<th>Base (eq.)</th>
<th>time</th>
<th>Yield [%][a]</th>
<th>d.r.[b]</th>
<th>Ee[c]</th>
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<td>A3 (5)</td>
<td>THF</td>
<td>K₂CO₃ (1.1)</td>
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<td>94</td>
<td>1:1.1</td>
<td>rac</td>
</tr>
<tr>
<td>2</td>
<td>A4 (5)</td>
<td>THF</td>
<td>K₂CO₃ (1.1)</td>
<td>24</td>
<td>96</td>
<td>1:1.7</td>
<td>rac</td>
</tr>
<tr>
<td>3</td>
<td>B1 (10)</td>
<td>THF</td>
<td>Cs₂CO₃ (1.1)</td>
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<td>90</td>
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<tr>
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<td>Cs₂CO₃ (0.1)</td>
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<td>&lt; 5</td>
<td>-</td>
<td>-</td>
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<tr>
<td>5</td>
<td>B3 (10)</td>
<td>dioxane</td>
<td>Cs₂CO₃ (0.1)</td>
<td>48</td>
<td>&lt; 5</td>
<td>-</td>
<td>-</td>
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<td>6</td>
<td>C1 (20)</td>
<td>THF</td>
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<td>48</td>
<td>&lt; 5</td>
<td>-</td>
<td>-</td>
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<td>THF</td>
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<td>72</td>
<td>&lt; 5</td>
<td>-</td>
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2.2 Influence of Catalyst Loading

![Catalyst Structure](image1.png)

**A1** (Ar = 3,4,5-F₃-C₆H₂)

**Catalyst Loading:**
- **5 mol% A1:** 97%, dr = 10:1, ee > 99.5%
- **0.5 mol% A1:** 98%, dr = 10:1, ee > 99.5%
- **0.1 mol% A1:** 99%, dr = 10:1, ee = 99.5%
- **0.01 mol% A1:** 98%, dr = 10:1, ee = 99.0%
- **0.002 mol% A1:** 90%, dr = 10:1, ee = 99.0%

![Chemical Reaction](image2.png)

**1a** 1.38 g (5 mmol)  
**2a** 2.21 g (7.5 mmol)  
**A1** (0.09 mg; 0.002 mol%)  
**Cs₂CO₃** (1.1 eq.)  
**Et₂O**  
-20 °C, 24-48 h  
**3a** 2.57 g; 4.5 mmol (90%)  
dr = 10:1, ee = 99%
3. Syntheses

3.1 Synthesis of 4-mono-substituted, N-protected Isoxazolidin-5-ones 1

Isoxazolidin-5-ones 1 were prepared according to the method reported by Briere and co-workers:

\[
\begin{align*}
\text{R}^1 & \quad \text{O} \quad \text{CO}_2 \text{R}^2 \\
\text{Ts} & \quad \text{HO} \quad \text{N} \quad \text{CO}_2 \text{R}^2 \\
\end{align*}
\]

General Procedure:
Meldrums acid derivative 9 (1.1 eq.), nitrone precursor 10 (1.0 eq) and K$_2$CO$_3$ (2.5 eq.) were suspended in THF (0.1 M) and stirred at room temperature for 24 h. The reaction mixture was filtered through a pad of Celite, washed with E$_2$O and the solvent was evaporated under reduced pressure. The crude product was subjected to column chromatography (silica gel, heptanes/EtOAc = 5/1).

Analytical data for new compounds 1 are given below.

**Compound 1d** (*tert*-butyl 4-(furan-2-ylmethyl)-5-oxoisoxazolidine-2-carboxylate): Prepared following the general procedure and obtained as a light-yellow oil (490 mg, 1.83 mmol, 70%). $R_f$ (heptanes/EtOAc = 5/1) = 0.35. $^1$H NMR (300 MHz, $\delta$, CDCl$_3$, 298 K): 7.37 – 7.31 (m, 1H), 6.34 – 6.27 (m, 1H), 6.16 – 6.10 (m, 1H), 4.36 – 4.27 (m, 1H), 3.76 – 3.67 (m, 1H), 3.29 – 3.18 (m, 2H), 2.95 – 2.84 (m, 1H), 1.52 (s, 9H). $^{13}$C NMR (75 MHz, $\delta$, CDCl$_3$, 298 K): 173.9, 155.9, 150.7, 142.3, 110.6, 107.6, 84.3, 53.3, 40.1, 28.1, 27.0. HRMS (ESI): calcd m/z for C$_{13}$H$_{17}$NO$_5$: 285.1445 [M+NH$_4]^+$; found: 285.1440.

**Compound 1k** (*tert*-butyl 4-(4-fluorobenzyl)-5-oxoisoxazolidine-2-carboxylate): Prepared following the general procedure and obtained as a colorless oil (522 mg, 1.77 mmol, 75%). $R_f$ (heptanes/EtOAc = 5/1) = 0.45. $^1$H NMR (300 MHz, $\delta$, CDCl$_3$, 298 K): 7.14 – 7.04 (m, 2H), 6.94 (t, $J$ = 8.5 Hz, 2H), 4.13 – 4.01 (m, 1H), 3.68 – 3.55 (m, 1H), 3.17 – 3.01 (m, 2H), 2.79 – 2.68 (m, 1H), 1.43 (s, 9H). $^{13}$C NMR (75 MHz, $\delta$, CDCl$_3$, 298 K): 178.7, 163.4 (d, $J$ = 245.5 Hz), 160.2 (d, $J$ = 245.5 Hz), 157.2, 134.0, 133.9, 130.6, 130.5, 130.5, 115.6, 115.3, 82.9, 51.5, 45.7, 34.5, 28.3. $^{19}$F NMR (282 MHz, $\delta$, CDCl$_3$, 298 K): -115.20 – -115.30 (m, 1F). HRMS (ESI): calcd m/z for C$_{15}$H$_{18}$FNO$_4$: 313.1564 [M+NH$_4]^+$; found: 313.1559.

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Compound 1n: \textit{(tert-butyl 4-(cyclohexylmethyl)-5-oxoisoxazolidine-2-carboxylate):} Prepared following the general procedure and obtained as a yellow oil (578 mg, 2.04 mmol, 68%). \( R_f \) (heptanes/EtOAc = 5/1) = 0.60. \(^1\)H NMR (300 MHz, \( \delta \), CDCl\(_3\), 298 K): 4.29 (dd, \( J = 10.9, 8.5 \text{ Hz}, 1\text{H} \)), 3.61 (dd, \( J = 11.0, 9.4 \text{ Hz}, 1\text{H} \)), 3.00 – 2.83 (m, 1H), 1.83 – 1.63 (m, 6H), 1.52 (s, 9H), 1.45 – 1.16 (m, 5H), 1.03 – 0.83 (m, 2H). \(^{13}\)C NMR (75 MHz, \( \delta \), CDCl\(_3\), 298 K): 175.6, 156.2, 84.1, 54.2, 38.2, 36.5, 35.6, 33.6, 32.4, 28.2, 26.4, 26.1, 26.1. HRMS (ESI): calcd \textit{m/z} for C\(_{15}\)H\(_{25}\)NO\(_4\): 301.2122 [M+NH\(_4\)]\(^+\); found: 301.2120.

Compound 1m: \textit{(tert-butyl 4-(cyclopropylmethyl)-5-oxoisoxazolidine-2-carboxylate):} Prepared following the general procedure and obtained as a colorless oil (389 mg, 1.61 mmol, 66%). \( R_f \) (heptanes/EtOAc = 5/1) = 0.50. \(^1\)H NMR (300 MHz, \( \delta \), CDCl\(_3\), 298 K): 4.40 – 4.28 (m, 1H), 3.77 (t, \( J = 10.2 \text{ Hz}, 1\text{H} \)), 3.04 – 2.88 (m, 1H), 1.79 – 1.70 (m, 1H), 1.50 (s, 9H), 1.48 – 1.40 (m, 1H), 0.80 – 0.66 (m, 1H), 0.57 – 0.44 (m, 2H), 0.17 – 0.04 (m, 2H). \(^{13}\)C NMR (75 MHz, \( \delta \), CDCl\(_3\), 298 K): 175.0, 156.1, 84.1, 53.4, 41.0, 33.6, 28.1, 8.7, 5.0, 4.4. HRMS (ESI): calcd \textit{m/z} for C\(_{12}\)H\(_{19}\)NO\(_4\): 259.1652 [M+NH\(_4\)]\(^+\); found: 301.2120.

### 3.2 Synthesis of CF\(_3\)-quinone methide 2x

CF\(_3\)-quinone methide precursor F was obtained following a modified procedure reported by Hamashima et al.\(^7\):

\[
\begin{array}{c}
\begin{array}{c}
\text{tBu} \quad \text{tBu} \\
\text{OH} \\
\end{array} \\
\text{Cul (0.1 eq.)} \\
\text{Togni II (1.5 eq.)} \\
\text{DMF, 40 °C, 1 h} \\
\end{array}
\quad
\begin{array}{c}
\begin{array}{c}
\text{tBu} \quad \text{tBu} \\
\text{OH} \\
\end{array} \\
\quad
\text{80%} \\
\end{array}
\quad
\begin{array}{c}
\begin{array}{c}
\text{tBu} \quad \text{tBu} \\
\text{OH} \\
\quad
\text{CF}_3 \\
\quad
\text{80%} \\
\end{array} \\
\text{DDQ (2.5 eq.)} \\
\text{MeOH, 1 h} \\
\end{array}
\quad
\begin{array}{c}
\begin{array}{c}
\text{tBu} \quad \text{tBu} \\
\quad
\text{CF}_3 \\
\quad
\text{99%} \\
\end{array} \\
\end{array}
\end{array}
\]

Cul (190 mg, 1.0 mmol) and Togni reagent II (4.74 g, 15.0 mmol) were dissolved in 50 mL DMF. Phenol 11 was added and the mixture was stirred for 1 h at 40 °C. The reaction mixture was subsequently diluted with EtOAc and washed with a saturated solution of NaHCO\(_3\). The organic layer was dried over Na\(_2\)SO\(_4\), filtered and concentrated \textit{in vacuo}. The crude product was purified by column chromatography on silica gel (DCM/heptanes = 4:1) to obtain product 12 in 80% yield. Spectroscopic data are consistent with those reported in the literature.

Phenol 12 (2.88 g, 10.0 mmol) was dissolved in 200 mL MeOH and DDQ (5.68 g, 25.0 mmol) was added. The reaction mixture was stirred at room temperature for 1 h. After completion of the reaction the solvent was evaporated and the crude reaction mixture was purified by column chromatography (heptanes/DCM = 10:1) to afford trifluoro-quinone methide in 92% yield.

CF₃-quinone methide 2x (2,6-di-tert-butyl-4-(2,2,2-trifluoroethylidene)cyclohexa-2,5-dien-1-one):
Prepared following the procedure described above and obtained as a yellow solid (2.63 g, 9.2 mmol, 92%). Rₜ (heptanes/dichloromethane = 4/1) = 0.50. m.p. = 34.5 – 35.0 °C. 1H NMR (300 MHz, δ, CDCl₃, 298 K): 7.33 (s, 1H), 6.78 (s, 1H), 6.03 (q, J = 8.9 Hz, 1H), 1.29 (s, 9H), 1.28 (s, 9H). 13C NMR (176 MHz, δ, CDCl₃, 298 K): 186.2, 151.7, 151.4, 138.4 (q, J = 5.5 Hz), 132.4, 125.3, 124.2 (q, J = 34.7 Hz), 123.0 (q, J = 271.0 Hz), 35.8, 35.4, 29.5. HRMS (ESI): calcd m/z for C₁₆H₂₁F₃O: 287.1623 [M+H]+; found: 287.1620.

### 3.3 Synthesis of racemic 4-disubstituted Isoxazolidin-5-ones 3

Isoxazolidinone D (1 eq.), p-quinone methide H (1.5 eq.), Cs₂CO₃ (1.1 eq.) and NEt₃BnCl (0.1 eq.) were suspended in Et₂O (0.1 M) and stirred overnight at room temperature. The reaction mixture was diluted with DCM, filtered through a short pad of silica (washed with DCM) and the solvent was evaporated to dryness in vacuo. The crude product was purified by column chromatography (silica gel, heptanes/EtOAc = 20/1 to 5/1) to obtain a diastereomeric mixture of racemic I. For final characterization, most diastereomers were separated by semi-preparative HPLC.

### 3.4 Asymmetric Synthesis of enantioenriched 4-disubstituted Isoxazolidin-5-ones 3 using Catalyst A1

---

S 10
Isoxazolidinone 1 (1 eq.), p-quinone methide 2 (1.5 eq.) and catalyst A1 (0.05 eq.) were suspended in Et₂O (0.1 M) and stirred at -20 °C for 20 min. Cs₂CO₃ (1.1 eq.) was added and the mixture was stirred for 24 h at -20°C. The reaction mixture was diluted with DCM, filtered through a short pad of silica (washed with DCM) and the solvent was evaporated to dryness in vacuo. The diastereomeric mixture of I was obtained by column chromatography (silica gel, heptanes/EtOAc = 20/1 to 5/1) and for most examples the diastereomers were further separated by semi-preparative HPLC to carry out the full characterization (silica gel, n-hexane/DCM). Analytical data for new compounds are given below.

Adduct 3a *(tert-butyl (S)-4-benzyl-4-((S)-(3,5-di-tert-butyl-4-hydroxyphenyl)(phenyl)methyl)-5-oxoisoxazolidine-2-carboxylate)*: Prepared following the general procedure and obtained as colorless crystals (55.5 mg, 0.097 mmol, 97%, d.r. = 10:1, >99.5% ee). m.p. = 140 – 142 °C. Rₜ (heptanes/EtOAc = 5/1) = 0.50. [a]ᵢ²³ (c = 1.00, CHCl₃) = +52.4°. ¹H NMR (700 MHz, δ, CDCl₃, 298 K): 7.30 – 7.27 (m, 4H), 7.25 – 7.08 (m, 4H), 7.02 (m, 4H), 7.19 (m, 4H), 7.08 (m, 1H), 4.26 (d, J = 13.8 Hz, 1H), 3.10 (d, J = 13.8 Hz, 1H), 2.87 (d, J = 13.8 Hz, 1H), 1.46 (s, 18H), 1.27 (s, 9H). ¹³C NMR (176 MHz, δ, CDCl₃, 298 K): 176.4, 154.3, 153.0, 139.7, 136.5, 135.0, 130.3, 129.8, 129.4, 128.8, 127.7, 127.4, 126.0, 83.2, 56.6, 55.6, 51.9, 43.3, 34.6, 30.5, 28.1. HRMS (ESI): calcd m/z 589.3636 [M+NH₄]⁺; found: 589.3633. HPLC (YMC CHIRAL ART Cellulose-SB, eluent: hexane/i-PrOH = 200:1, 0.5 mL/min, 10 °C) retention times: tᵣₗᵢₐ₉ = 21.3 min, tᵣᵢₗₘ₀ᵢ₉ = 30.8 min.

Adduct 3b *(tert-butyl (S)-4-[(1,1′-biphenyl)-4-ylmethyl]-4-((S)-(3,5-di-tert-butyl-4-hydroxyphenyl)(phenyl)methyl)-5-oxoisoxazolidine-2-carboxylate)*: Prepared according the general procedure and obtained as a colorless crystals (64.1 mg, 0.099 mmol, 99%, d.r. = 10:1, >99.5% ee). m.p. = 166 – 168 °C. Rₜ (heptanes/EtOAc = 5/1) = 0.45. [a]ᵢ²³ (c = 0.70, CHCl₃) = +64.1°; ¹H NMR (700 MHz, δ, CDCl₃, 298 K): 7.57 – 7.54 (m, 2H), 7.50 (d, J = 8.0 Hz, 2H), 7.41 (t, J = 7.7 Hz, 2H), 7.34 – 7.31 (m,
3H), 7.30 – 7.27 (m, 2H), 7.22 – 7.19 (m, 1H), 7.13 (d, $J = 8.4$ Hz, 2H), 5.19 (s, 1H), 4.54 (s, 1H), 4.50 (d, $J = 10.6$ Hz, 1H), 4.31 (d, $J = 10.6$ Hz, 1H), 3.14 (d, $J = 14.0$ Hz, 1H), 2.93 (d, $J = 14.0$ Hz, 1H), 1.47 (s, 18H), 1.25 (s, 8H). $^{13}$C NMR (176 MHz, $\delta$, CDCl$_3$, 298 K): 176.4, 154.4, 153.1, 140.6, 140.3, 139.7, 136.5, 134.1, 130.8, 129.8, 129.4, 128.9, 128.8, 127.5, 127.4, 127.1, 126.0, 83.3, 56.6, 55.6, 52.0, 42.9, 34.6, 30.5, 28.1. HRMS (ESI): calcd $m/z$ for C$_{36}$H$_{47}$NO$_5$: 665.3949 [M+NH$_4$]$^+$; found: 665.3946. HPLC (YMC CHIRAL ART Amylose-SA, eluent: hexane/i-PrOH = 50:1, 0.5 mL/min, 10 °C) retention times: $t_{\text{minor}} = 27.1$ min, $t_{\text{major}} = 18.3$ min.

**racemic 3b**

**scalemic 3b**

Adduct 3c  

(tert-buty1 (S)-4-[(S)-(3,5-di-tert-butyl-4-hydroxyphenyl)(phenyl)methyl)-4-(naphthalen-2-ylmethyl)-5-oxoisoxazolidine-2-carboxylate):

Prepared following the general procedure and obtained as a colorless powder (60.3 mg, 0.097 mmol, 97%, d.r. = 10:1, >99.5% ee). m.p. = 161 – 163 °C. $R_l$ (heptanes/EtOAc = 5/1) = 0.50. $[\alpha]_D^{23}$ (c = 0.70, CHCl$_3$) = +87.9°; $^1$H NMR (700 MHz, $\delta$, CDCl$_3$, 298 K): 7.79 – 7.76 (m, 2H), 7.75 (d, $J = 8.5$ Hz, 1H), 7.54 – 7.52 (m, 1H), 7.47 – 7.42 (m, 2H), 7.34 – 7.32 (m, 2H), 7.31 – 7.27 (m, 2H), 7.22 – 7.18 (m, 2H), 7.09 (s, 2H), 5.22 (s, 1H), 4.57 (s, 1H), 4.50 (d, $J = 10.6$ Hz, 1H), 4.36 (d, $J = 10.5$ Hz, 1H), 3.28 (d, $J = 14.0$ Hz, 1H), 3.05 (d, $J = 14.0$ Hz, 1H), 1.48 (s, 18H), 1.06 (s, 9H). $^{13}$C NMR (176 MHz, $\delta$, CDCl$_3$, 298 K): 176.6, 154.2, 153.1, 139.7, 136.5, 133.5, 132.8, 132.6, 129.8, 129.5, 129.2, 128.8, 128.5, 128.2, 128.1, 127.8, 127.4, 126.3, 126.1, 126.0, 83.2, 56.7, 55.7, 51.9, 43.3, 34.6, 30.6, 27.8. HRMS (ESI): calcd $m/z$ for C$_{49}$H$_{59}$NO$_7$: 639.3792 [M+NH$_4$]$^+$; found: 639.3797. HPLC (YMC CHIRAL ART Cellulose-SB, eluent: hexane/i-PrOH = 200:1, 0.5 mL/min, 10 °C) retention times: $t_{\text{minor}} = 38.1$ min, $t_{\text{major}} = 46.4$ min.
Adduct 3d (tert-butyl (S)-4-((S)-(3,5-di-tert-butyl-4-hydroxyphenyl)(phenyl)methyl)-4-(furan-2-ylmethyl)-5-oxoisoxazolidine-2-carboxylate): Prepared following the general procedure and obtained as a colorless oil (55.0 mg, 0.098 mmol, 98%, d.r. = 11:1, >99.5% ee). Rf (heptanes/EtOAc = 5/1) = 0.30. [α]D23 (c = 0.50, CHCl3) = 34.9°; 1H NMR (300 MHz, δ, CDCl3, 298 K): 7.32 – 7.28 (m, 5H), 7.03 (s, 2H), 6.29 – 6.24 (m, 1H), 6.08 (d, J = 3.3 Hz, 1H), 5.19 (s, 1H), 4.52 – 4.46 (m, 2H), 4.25 (d, J = 10.6 Hz, 1H), 3.09 – 2.98 (m, 1H), 1.44 (s, 18H), 1.35 (s, 9H). 13C NMR (75 MHz, δ, CDCl3, 298 K): 176.1, 154.4, 153.1, 149.7, 142.7, 139.5, 136.4, 129.6, 129.1, 128.8, 127.4, 125.9, 110.7, 109.2, 83.3, 56.4, 54.5, 52.5, 36.1, 34.5, 30.4, 28.2. HRMS (ESI): calcd m/z for C34H43NO6: 579.3429 [M+NH4]+; found: 579.3430. HPLC (YMC CHIRAL ART Cellulose-SB, eluent: hexane:i-PrOH = 200:1, 0.5 mL/min, 10 °C) retention times: tminor = 24.4 min, tmajor = 26.7 min.
Adduct 3e (tert-butyl ((S)-(3,5-di-tert-butyl-4-hydroxyphenyl)phenyl)methyl)-4-(4-methylbenzyl)-5-oxoisoxazolidine-2-carboxylate: Prepared following the general procedure and obtained as a colorless solid (56.8 mg, 0.097 mmol, 97%, d.r. = 10:1, >99.5% ee). m.p. = 154 – 155 °C. Rf (heptanes/EtOAc = 5/1) = 0.50. [α]D 23 (c = 1.00, CHCl3) = +59.6°. 1H NMR (300 MHz, δ, CDCl3, 298 K): 7.30 – 7.19 (m, 5H), 7.10 – 7.01 (m, 4H), 6.95 (d, J = 7.9 Hz, 2H), 5.19 (s, 1H), 4.56 – 4.42 (m, 2H), 4.27 (d, J = 10.6 Hz, 1H), 3.07 (d, J = 13.8 Hz, 1H), 2.83 (d, J = 13.8 Hz, 1H), 2.28 (s, 3H), 1.46 (s, 18H), 1.28 (s, 9H). 13C NMR (75 MHz, δ, CDCl3, 298 K): 176.6, 154.3, 153.0, 139.8, 137.2, 136.4, 131.9, 130.1, 129.8, 129.5, 129.5, 128.8, 127.3, 126.0, 83.2, 56.6, 55.6, 51.8, 42.9, 34.6, 30.5, 28.1, 21.2. HRMS (ESI): calcd m/z for C37H47NO5: 603.3792 [M+NH4]+; found: 603.3788. HPLC (YMC CHIRAL ART Cellulose-SB, eluent: hexane/i-PrOH = 200:1, 0.5 mL/min, 10 °C) retention times: tminor = 20.1 min, tmajor = 24.0 min.

Adduct 3f (tert-butyl ((S)-(3,5-di-tert-butyl-4-hydroxyphenyl)phenyl)methyl)-4-(2-methylbenzyl)-5-oxoisoxazolidine-2-carboxylate: Prepared following the general procedure and obtained as a colorless oil (56.2 mg, 0.096 mmol, 96%, d.r. = 3:1, >99.5% ee). Rf (heptanes/EtOAc = 5/1) = 0.55. [α]D 23 (c = 0.70, CHCl3) = +47.4°. 1H NMR (700 MHz, δ, CDCl3, 298 K): 7.38 – 7.34 (m, 2H), 7.31 – 7.27 (m, 2H), 7.23 – 7.19 (m, 1H), 7.14 – 7.09 (m, 6H), 5.20 (s, 1H), 4.53 (s, 1H), 4.51 (d, J = 10.6 Hz, 1H), 4.06 (d, J = 10.6 Hz, 1H), 3.06 – 2.98 (m, 2H), 2.13 (s, 3H), 1.46 (s, 18H), 1.26 (s, 9H). 13C NMR (176 MHz, δ, CDCl3, 298 K): 177.2, 154.0, 153.2, 139.4, 137.0, 136.5, 133.8, 130.9, 130.3, 129.7, 128.9, 127.4, 126.6, 125.9, 83.2, 57.2, 55.9, 39.1, 34.6, 30.4, 28.2, 20.3. HRMS (ESI): calcd m/z for C37H47NO5: 603.3792 [M+NH4]+; found: 603.3788. HPLC (YMC CHIRAL ART Cellulose-SB, eluent: hexane/i-PrOH = 200:1, 0.5 mL/min, 10 °C) retention times: tminor = 20.9 min, tmajor = 30.3 min.
Adduct 3g (tert-butyl (S)-4-(4-(tert-butyl)benzyl)-4-((S)-(3,5-di-tert-butyl-4-hydroxyphenyl)-(phenyl)methyl)-5-oxoisoxazolidine-2-carboxylate): Prepared following the general procedure and obtained as a colorless oil (59.0 mg, 0.094 mmol, 94%, d.r. = 14:1, >99.5% ee). Rf (heptanes/EtOAc = 5/1) = 0.55. [α]D23 (c = 0.85, CHCl3) = 104.0°. 1H NMR (700 MHz, δ, CDCl3, 298 K): 7.32 – 7.26 (m, 6H), 7.22 – 7.17 (m, 1H), 7.04 (s, 2H), 6.97 (d, J = 8.3 Hz, 2H), 5.19 (s, 1H), 4.52 – 4.48 (m, 2H), 4.24 (d, J = 10.5 Hz, 1H), 3.07 (d, J = 14.1 Hz, 1H), 2.86 (d, J = 14.1 Hz, 1H), 1.45 (s, 18H), 1.29 (s, 9H), 1.27 (s, 9H). 13C NMR (176 MHz, δ, CDCl3, 298 K): 176.4, 154.4, 153.0, 150.3, 139.8, 136.4, 132.0, 130.1, 129.8, 129.5, 128.8, 127.3, 126.0, 125.7, 83.2, 60.5, 56.5, 55.4, 52.2, 42.6, 34.6, 34.6, 31.4, 30.5, 28.2. HRMS (ESI): calcd m/z for C40H53NO5: 645.4262 [M+NH4]⁺; found: 645.4257. HPLC (YMC CHIRAL ART Cellulose-SB, eluent: hexane:i-PrOH = 300:1, 0.5 mL/min, 10 °C) retention times: tminor = 31.3 min, tmajor = 34.0 min.
Adduct 3h (tert-butyl (S)-4-((S)-(3,5-di-tert-butyl-4-hydroxyphenyl)(phenyl)methyl)-4-(4-methoxybenzyl)-5-oxoisoxazolidine-2-carboxylate): Prepared following the general procedure and obtained as a colorless oil (59.3 mg, 0.099 mmol, 99%, d.r. = 9:1, >99.5% ee).

R<sub>t</sub> (heptanes/EtOAc = 5/1) = 0.30. [α]<sub>D</sub><sup>23</sup> (c = 0.70, CHCl<sub>3</sub>) = 114.1°. 1H NMR (300 MHz, δ, CDCl<sub>3</sub>, 298 K): 7.26 – 7.15 (m, 5H), 7.03 – 6.93 (m, 4H), 6.81 – 6.72 (m, 2H), 4.51 – 4.41 (m, 2H), 4.24 (d, J = 10.4 Hz, 1H), 3.72 (s, 3H), 3.01 (d, J = 14.0 Hz, 1H), 2.78 (d, J = 14.0 Hz, 1H), 1.43 (s, 18H), 1.25 (s, 9H). 13C NMR (75 MHz, δ, CDCl<sub>3</sub>, 298 K): 176.6, 159.0, 154.3, 153.0, 139.8, 136.4, 131.3, 129.7, 129.5, 128.8, 127.4, 125.9, 126.0, 114.2, 83.2, 56.5, 55.7, 55.2, 51.8, 42.6, 34.6, 30.5, 28.1. HRMS (ESI): calcd m/z for C<sub>37</sub>H<sub>47</sub>N<sub>6</sub>O<sub>6</sub>: 619.3742 [M+NH<sub>4</sub>]<sup>+</sup>; found: 619.3746.

HPLC (YMC CHIRAL ART Cellulose-SB, eluent: hexane/i-PrOH = 30:1, 0.5 mL/min, 10 °C) retention times: t<sub>minor</sub> = 13.9 min, t<sub>major</sub> = 15.5 min.

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Adduct 3i (tert-butyl (S)-4-(4-chlorobenzyl)-4-((S)-(3,5-di-tert-butyl-4-hydroxyphenyl)(phenyl)methyl)-5-oxoisoxazolidine-2-carboxylate): Prepared following the general procedure and obtained as a colorless solid (59.0 mg, 0.097 mmol, 97%, d.r. = 8:1, 99.3% ee). m.p. = 178 – 180 °C.

R<sub>t</sub> (heptanes/EtOAc = 5/1) = 0.45. [α]<sub>D</sub><sup>23</sup> (c = 0.95, CHCl<sub>3</sub>) = 88.4°. 1H NMR (300 MHz, δ, CDCl<sub>3</sub>, 298 K): 7.32 – 7.17 (m, 7H), 7.06 – 6.94 (m, 4H), 5.20 (s, 1H), 4.55 – 4.39 (m, 2H), 4.24 (d, J = 10.4 Hz, 1H), 3.05 (d, J = 14.0 Hz, 1H), 2.84 (d, J = 13.8 Hz, 1H), 1.46 (s, 18H), 1.30 (s, 9H). 13C NMR (75 MHz, δ, CDCl<sub>3</sub>, 298 K): 176.2, 154.3, 139.5, 136.6, 133.7, 133.5, 131.6, 129.8, 129.2, 129.0, 128.8, 127.4, 125.9, 83.6, 56.5, 55.5, 51.9, 42.6, 34.6, 31.7, 30.5, 28.1, 22.8, 14.3. HRMS (ESI): calcd m/z for C<sub>35</sub>H<sub>44</sub>ClNO<sub>5</sub>: 623.3246 [M+NH<sub>4</sub>]<sup>+</sup>; found: 623.3242.

HPLC (YMC CHIRAL ART Cellulose-SB, eluent: hexane/i-PrOH = 200:1, 0.5 mL/min, 10 °C) retention times: t<sub>minor</sub> = 20.0 min, t<sub>major</sub> = 24.7 min.
Adduct 3j: (tert-butyl) (S)-4-(4-bromobenzyl)-4-((S)-(3,5-di-tert-butyl-4-hydroxyphenyl) (phenyl)methyl)-5-oxoisoxazolidine-2-carboxylate: Prepared following the general procedure and obtained as colorless crystals (61.8 mg, 0.095 mmol, 95%, d.r. = 7:1, 99.4% ee). m.p. = 170 – 172 °C. Rf (heptanes/EtOAc = 5/1) = 0.50. [α]D23 (c = 1.00, CHCl3) = +30.9°. 1H NMR (300 MHz, δ, CDCl3, 298 K): 7.42 – 7.34 (m, 2H), 7.31 – 7.19 (m, 6H), 7.02 (s, 2H), 6.97 – 6.89 (m, 2H), 5.21 (s, 1H), 4.53 – 4.42 (m, 2H), 4.24 (d, J = 10.7 Hz, 1H), 3.03 (d, J = 13.6 Hz, 1H), 2.83 (d, J = 13.7 Hz, 1H), 1.45 (s, 18H), 1.30 (s, 9H). 13C NMR (75 MHz, δ, CDCl3, 298 K): 176.2, 154.3, 153.1, 139.5, 136.5, 134.0, 132.0, 131.9, 129.8, 129.2, 128.8, 127.4, 125.9, 121.9, 83.6, 56.5, 55.5, 51.9, 42.7, 34.6, 30.5, 28.1. HRMS (ESI): calcd m/z for C36H44BrNO5: 667.2744 [M+NH4]+; found: 667.2741. HPLC (YMC CHIRAL ART Cellulose-SB, eluent: hexane/i-PrOH = 200:1, 0.5 mL/min, 10 °C) retention times: tminor = 26.2 min, tmajor = 31.2 min.
Adduct 3k (tert-butyl (S)-4-((S)-(3,5-di-tert-butyl-4-hydroxyphenyl)(phenyl)methyl)-4-(4-fluorobenzyl)-5-oxoisoxazolidine-2-carboxylate): Prepared following the general procedure and obtained as a colorless oil (58.6 mg, 0.099 mmol, 99%, d.r. = 7:1, 99.1% ee). R_f (heptanes/EtOAc = 5/1) = 0.55. [α]_D^23 (c = 0.80, CHCl_3) = 51.4°. 1H NMR (700 MHz, δ, CDCl_3, 298 K): 7.28 (d, J = 4.3 Hz, 4H), 7.23 – 7.19 (m, 1H), 7.04 – 7.01 (m, 4H), 6.95 (t, J = 8.6 Hz, 2H), 5.20 (s, 1H), 4.51 (s, 1H), 4.46 (d, J = 10.6 Hz, 1H), 4.25 (d, J = 10.6 Hz, 1H), 3.05 (d, J = 14.1 Hz, 1H), 2.84 (d, J = 14.1 Hz, 1H), 1.46 (s, 18H), 1.29 (s, 9H). 13C NMR (176 MHz, δ, CDCl_3, 298 K): 176.3, 163.1, 161.7, 154.3, 153.1, 139.6, 136.5, 131.9, 131.8, 130.7, 130.7, 129.7, 129.3, 128.8, 127.4, 125.9, 115.8, 115.7, 83.5, 56.5, 55.6, 51.9, 42.5, 34.6, 30.5, 28.1. 19F NMR (282 MHz, δ, CDCl_3, 298 K): -114.84 – -114.94 (m, 1F). HRMS (ESI): calcd m/z for C_{36}H_{44}FNO_6: 607.3542 [M+NH_4]^+; found: 607.3534. HPLC (YMC CHIRAL ART Cellulose-SB, eluent: hexane:i-PrOH = 200:1, 0.5 mL/min, 10 °C) retention times: t_{minor} = 18.2 min, t_{major} = 28.8 min.

racemic 3k

scalemic 3k

Adduct 3l (tert-butyl (S)-4-cinnamyl-4-((S)-(3,5-di-tert-butyl-4-hydroxyphenyl)(phenyl)methyl)-5-oxoisoxazolidine-2-carboxylate): Prepared following the general procedure and obtained as a colorless oil (56.7 mg, 0.095 mmol, 95%, d.r. = 9:1, 99.4% ee). R_f (heptanes/EtOAc = 5/1) = 0.55. [α]_D^23 (c = 0.55, CHCl_3) = +75.5°. 1H NMR (700 MHz, δ, CDCl_3, 298 K): 7.31 – 7.21 (m, 8H), 7.21 – 7.19 (m, 1H), 7.07 – 7.05 (m, 4H), 6.15 (d, J = 15.7 Hz, 1H), 6.04 – 5.94 (m, 1H), 5.20 (s, 1H), 4.53 (s, 1H), 4.48 (d, J = 10.4 Hz, 1H), 4.27 (d, J = 10.6 Hz, 1H), 2.49 – 2.46 (m, 2H), 1.46 (s, 1H), 1.28 (s, 9H). 13C NMR (176 MHz, δ, CDCl_3, 298 K): 176.4, 154.3, 153.0, 139.7, 136.4, 136.0, 135.0, 130.3, 129.8, 129.4, 128.8, 127.7, 127.3, 126.0, 123.8, 83.3, 56.6, 55.6, 51.9, 43.3, 34.6, 30.5, 28.1. HRMS (ESI): calcd m/z for C_{38}H_{47}NO_5: 615.3792 [M+NH_4]^+; found: 615.3785. HPLC (YMC CHIRAL ART
Cellulose-SB, eluent: hexane:i-PrOH = 200:1, 0.5 mL/min, 10 °C) retention times: \( t_{\text{minor}} = 21.5 \text{ min} \), \( t_{\text{major}} = 30.3 \text{ min} \).

Adduct 3m (tert-butyl (S)-4-(cyclopropylmethyl)-4-((S)-(3,5-di-tert-butyl-4-hydroxyphenyl)-(phenyl)methyl)-5-oxoisoxazolidine-2-carboxylate): Prepared following the general procedure and obtained as a colorless oil (50.4 mg, 0.090 mmol, 90%, d.r. = 9:1, 98.0% ee). \( R_f \) (heptanes/EtOAc = 5/1) = 0.45. \([\alpha]_D^23\) = 0.70, CHCl₃ = +18.3°.

\(^1\)H NMR (700 MHz, \( \delta \), CDCl₃, 298 K): 7.28 – 7.26 (m, 3H), 7.26 – 7.25 (m, 1H), 7.22 – 7.17 (m, 1H), 6.95 (s, 2H), 5.14 (s, 1H), 4.46 – 4.42 (m, 2H), 4.39 – 4.35 (m, 1H), 1.69 (dd, \( J = 14.4, 6.3 \text{ Hz} \), 1H), 1.50 (dd, \( J = 14.5, 7.5 \text{ Hz} \), 1H), 1.42 (s, 27H), 0.70 – 0.64 (m, 1H), 0.51 – 0.43 (m, 2H), 0.10 – 0.05 (m, 1H), 0.04 – 0.00 (m, 1H). \(^{13}\)C NMR (176 MHz, \( \delta \), CDCl₃, 298 K): 177.0, 155.4, 152.9, 139.9, 136.2, 129.7, 129.5, 128.7, 127.2, 125.9, 83.5, 56.3, 54.2, 53.4, 42.4, 34.5, 30.5, 28.2, 6.3, 5.0, 4.6. HRMS (ESI): calcd \( m/z \) for C₃₃H₄₅NO₅: 553.3636 [M+NH₄]⁺; found: 553.3641.

HPLC (YMC CHIRAL ART Cellulose-SB, eluent: hexane:i-PrOH = 200:1, 0.5 mL/min, 10 °C) retention times: \( t_{\text{minor}} = 16.5 \text{ min} \), \( t_{\text{major}} = 18.21 \text{ min} \).
Adduct 3n: (tert-butyl (S)-4-(cyclohexylmethyl)-4-((S)-(3,5-di-tert-butyl-4-hydroxyphenyl)-(phenyl)methyl)-5-oxoisoxazolidine-2-carboxylate): Prepared following the general procedure and obtained as a colorless oil (52.5 mg, 0.091 mmol, 91%, d.r. = 7:1, >99.5% ee). R<sub>f</sub> (heptanes/EtOAc = 5/1) = 0.55. [α]<sup>D</sup><sub>23</sub> (c = 0.35, CHCl<sub>3</sub>) = +44.9°. 

1H NMR (700 MHz, δ, CDCl<sub>3</sub>, 298 K): 7.30 – 7.26 (m, 4H), 7.21 – 7.17 (m, 1H), 6.96 (s, 2H), 5.14 (d, J = 10.6 Hz, 1H), 4.11 (d, J = 10.5 Hz, 1H), 1.66 – 1.62 (m, 1H), 1.62 – 1.55 (m, 5H), 1.43 (s, 9H), 1.42 (s, 18H), 1.35 – 1.32 (m, 1H), 1.29 – 1.13 (m, 3H), 1.08 – 1.02 (m, 1H), 0.87 – 0.82 (m, 1H), 0.80 – 0.74 (m, 1H). 

13C NMR (176 MHz, δ, CDCl<sub>3</sub>, 298 K): 176.9, 155.5, 152.9, 139.9, 136.2, 129.8, 129.4, 128.7, 127.2, 126.1, 83.6, 56.1, 54.5, 52.9, 44.5, 35.3, 34.5, 34.5, 33.7, 30.5, 28.2, 26.5, 26.4, 26.1. HRMS (ESI): calcd m/z for C<sub>36</sub>H<sub>51</sub>NO<sub>5</sub>: 595.4105 [M+NH<sub>4</sub>]<sup>+</sup>; found: 595.4112.

HPLC (YMC CHIRAL ART Amylose-SA, eluent: hexane:i-PrOH = 200:1, 0.5 mL/min, 10 °C) retention times: t<sub>minor</sub> = 32.2 min, t<sub>major</sub> = 37.4 min.

racemic 3n

Adduct 3o: (tert-butyl (S)-4-benzyl-4-((S)-(4-hydroxy-3,5-diisopropylphenyl)(phenyl)methyl)-5-oxoisoxazolidine-2-carboxylate): Prepared following the general procedure and obtained as a colorless oil (49.0 mg, 0.090 mmol, 90%, d.r. = 5:1, 98.9% ee). R<sub>f</sub> (heptanes/EtOAc = 5/1) = 0.35. [α]<sup>D</sup><sub>23</sub> (c = 0.70, CHCl<sub>3</sub>) = +139.0°. 

1H NMR (300 MHz, δ, CDCl<sub>3</sub>, 298 K): 7.32 – 7.27 (m, 4H), 7.26 – 7.18 (m, 4H), 7.11 – 7.02 (m, 2H), 6.94 (s, 2H), 4.80 (s, 1H), 4.56 (s, 1H), 4.49 (d, J = 10.6 Hz, 1H), 4.27 (d, J = 10.7 Hz, 1H), 3.24 – 3.07 (m, 3H), 2.85 (d, J = 13.8 Hz, 1H), 1.36 – 1.19 (m, 21H). 

13C NMR (75 MHz, δ, CDCl<sub>3</sub>, 298 K): 176.5, 154.3, 149.3, 139.6, 135.0, 134.4, 130.7, 130.3, 129.7, 128.8, 127.4, 124.6, 83.3, 56.6, 55.7, 51.8, 43.2, 28.1, 27.4, 23.0, 22.9. HRMS (ESI): calcd m/z for C<sub>34</sub>H<sub>35</sub>NO<sub>6</sub> [M+NH<sub>4</sub>]<sup>+</sup>; found: 561.3324. HPLC (YMC CHIRAL ART Cellulose-SB, eluent: hexane:i-PrOH = 200:1, 0.5 mL/min, 10 °C) retention times: t<sub>minor</sub> = 20.2 min, t<sub>major</sub> = 25.5 min.
Adduct 3p (tert-butyl) (S)-4-benzyl-4-[(S)-(3-tert-butyl)-4-hydroxy-5-methylphenyl]-(phenyl)methyl]-5-oxoisoxazolidine-2-carboxylate: Prepared following the general procedure and obtained as a colorless powder (52.3 mg, 0.099 mmol, 99%, d.r. = 10:1, 99.5% ee). m.p. = 117 – 120 °C. Rf (heptanes/EtOAc = 5/1) = 0.40. [α]D23 (c = 1.00, CHCl3) = +111.3°. 1H NMR (300 MHz, δ, CDCl3, 298 K): 7.32 – 7.27 (m, 4H), 7.26 – 7.16 (m, 4H), 7.10 – 7.02 (m, 3H), 6.90 (d, J = 2.3 Hz, 1H), 4.80 (s, 1H), 4.50 (d, J = 11.1 Hz, 2H), 4.27 (d, J = 10.6 Hz, 1H), 3.12 (d, J = 13.7 Hz, 1H), 2.88 (d, J = 13.7 Hz, 1H), 2.27 (s, 3H), 1.43 (s, 9H), 1.27 (s, 9H). 13C NMR (75 MHz, δ, CDCl3, 298 K): 176.3, 154.3, 152.0, 139.6, 136.3, 135.0, 130.3, 130.1, 129.7, 129.4, 128.8, 127.7, 127.4, 126.3, 123.8, 83.3, 56.3, 55.5, 51.8, 43.3, 34.8, 29.9, 28.1, 16.4. HRMS (ESI): calcd m/z for C33H39NO6: 547.3166 [M+NH4]+; found: 547.3163. HPLC (YMC CHIRAL ART Cellulose-SB, eluent: hexane/i-PrOH = 30:1, 0.5 mL/min, 10 °C) retention times: tminor = 32.5 min, tmajor = 51.1 min.
Adduct 3q \((\text{ tert-butyl})\) \((S)-4\text{-benzyl}-4-((S)-(3,5\text{-di-tert-butyl}-4\text{-hydroxyphenyl})(4\text{-methoxyphenyl})\text{methyl})-5\text{-oxoisoxazolidine-2-carboxylate}\): Prepared following the general procedure and obtained as a colorless oil (57.3 mg, 0.095 mmol, 95%, d.r. = 6:1, 99.1% ee). 

Rf (heptanes/EtOAc = 5/1) = 0.30. \([\alpha]_D^{23}\) (c = 0.60, CHCl3) = +67.2°. 

1H NMR (700 MHz, δ, CDCl3, 298 K): 7.28 – 7.25 (m, 3H), 7.24 – 7.21 (m, 1H), 7.20 (d, \(J = 8.8\) Hz, 2H), 7.06 (d, \(J = 7.2\) Hz, 2H), 7.02 (s, 2H), 6.80 (d, \(J = 8.8\) Hz, 2H), 5.18 (s, 1H), 4.51 – 4.47 (m, 2H), 4.25 (d, \(J = 10.5\) Hz, 1H), 3.74 (s, 3H), 3.09 (d, \(J = 14.0\) Hz, 1H), 2.86 (d, \(J = 13.9\) Hz, 1H), 1.46 (s, 18H), 1.28 (s, 9H). 

13C NMR (176 MHz, δ, CDCl3, 298 K): 176.6, 158.7, 154.3, 152.9, 136.4, 135.1, 131.7, 130.8, 130.3, 129.7, 128.8, 127.7, 125.8, 114.1, 83.2, 55.9, 55.8, 55.2, 51.7, 43.2, 34.6, 34.5, 30.5, 28.1. HRMS (ESI): calcd \(m/z\) for C\(_{37}\)H\(_{47}\)NO\(_6\): 619.3742 [M+NH\(_4\)]\(^+\); found: 619.3746. 

HPLC (YMC CHIRAL ART Cellulose-SB, eluent: hexane:i-PrOH = 30:1, 0.5 mL/min, 10°C) retention times: \(t_{\text{minor}} = 13.9\) min, \(t_{\text{major}} = 16.1\) min.

Adduct 3r \((\text{ tert-butyl})\) \((S)-4\text{-benzyl}-4-((R)-(3,5\text{-di-tert-butyl}-4\text{-hydroxyphenyl})(2\text{-methoxyphenyl})\text{methyl})-5\text{-oxoisoxazolidine-2-carboxylate}\): Prepared following the general procedure and obtained as a colorless oil (59.4 mg, 0.099 mmol, 99%, d.r. = 6:1, >99.5% ee). 

Rf (heptanes/EtOAc = 5/1) = 0.30. \([\alpha]_D^{23}\) (c = 0.65, CHCl3) = +59.0°. 

1H NMR (700 MHz, δ, CDCl3, 298 K): 7.81 – 7.77 (m, 1H), 7.26 – 7.19 (m, 4H), 7.14 (s, 2H), 7.08 – 7.04 (m, 2H), 7.00 – 6.95 (m, 1H), 6.86 – 6.82 (m, 1H), 5.11 (s, 1H), 4.81 (s, 1H), 4.34 (d, \(J = 10.8\) Hz, 1H), 4.08 (d, \(J = 10.8\) Hz, 1H), 3.76 (s, 3H), 3.15 (d, \(J = 13.8\) Hz, 1H), 2.96 (d, \(J = 13.9\) Hz, 1H), 1.41 (s, 18H), 1.30 (s, 9H). 

13C NMR (176 MHz, δ, CDCl3, 298 K): 176.0, 157.0, 154.0, 152.9, 135.8, 135.3, 130.5, 130.1, 129.9, 129.0, 128.7, 128.2, 127.5, 126.5, 120.9, 111.2, 83.0, 55.5, 54.4, 53.7, 49.3, 42.4, 34.5, 30.5, 28.2. HRMS
(ESI): calcd m/z for C_{37}H_{47}NO_{6}: 619.3742 [M+NH\textsubscript{4}]\textsuperscript{+}; found: 619.3746. HPLC (YMC CHIRAL ART Cellulose-SB, eluent: hexane:i-PrOH = 30:1, 0.5 mL/min, 10 °C) retention times: t\textsubscript{minor} = 12.7 min, t\textsubscript{major} = 14.6 min.

**racemic 3r**

**scalemic 3r**

Adduct 3s (**tert**-butyl (**S**)-4-benzyl-4-((**S**)-(4-chlorophenyl)(3,5-**tert**-butyl-4-hydroxyphenyl)-methyl)-5-oxoisoxazolidine-2-carboxylate): Prepared following the general procedure and obtained as a colorless oil (60.2 mg, 0.099 mmol, 99%, d.r. = 20:1, >99.5% ee). R\textsubscript{t} (heptanes/EtOAc = 5/1) = 0.50. [\alpha]\textsubscript{D}<sup>23</sup> (c = 1.00, CHCl\textsubscript{3}) = +98.1°. \textsuperscript{1}H NMR (700 MHz, δ, CDCl\textsubscript{3}, 298 K): 7.28 – 7.26 (m, 2H), 7.25 – 7.21 (m, 5H), 7.06 – 7.03 (m, 2H), 7.00 (s, 2H), 5.22 (s, 1H), 4.48 (s, 1H), 4.26 (d, J = 10.6 Hz, 1H), 4.26 (d, J = 10.6 Hz, 1H), 3.10 (d, J = 13.9 Hz, 1H), 2.89 (d, J = 14.0 Hz, 1H), 1.45 (s, 18H), 1.29 (s, 9H), \textsuperscript{13}C NMR (176 MHz, δ, CDCl\textsubscript{3}, 298 K): 176.4, 154.3, 153.2, 138.3, 136.7, 134.8, 133.3, 131.3, 130.3, 129.0, 129.0, 128.8, 127.8, 125.8, 83.5, 55.9, 55.5, 51.8, 43.1, 34.6, 30.5, 28.1. HRMS (ESI): calcd m/z for C_{36}H_{44}ClNO_{5}: 623.3246 [M+NH\textsubscript{4}]\textsuperscript{+}; found: 623.3242. HPLC (YMC CHIRAL ART Cellulose-SB, eluent: hexane:i-PrOH = 200:1, 0.5 mL/min, 10 °C) retention times: t\textsubscript{minor} = 30.2 min, t\textsubscript{major} = 34.1 min.

**racemic 3s**

**scalemic 3s**
Adduct 3s-Cbz (benzyl (S)-4-benzyl-4-((S)-(3,5-di-tert-butyl-4-hydroxyphenyl)methyl)-5-oxoisoxazolidine-2-carboxylate): Prepared following the general procedure and obtained as a colorless solid (22.7 mg, 0.035 mmol, 35%, d.r. = 14:1). m.p. = 134 – 136 °C. 

Rf (heptanes/EtOAc = 5/1) = 0.45. [α]D23 (c = 0.25, CHCl3) = +21.8°. 

1H NMR (700 MHz, δ, CDCl3, 298 K): 7.35 – 7.27 (m, 4H), 7.25 – 7.18 (m, 8H), 7.10 – 7.04 (m, 2H), 7.01 (s, 2H), 5.23 (s, 1H), 4.82 – 4.73 (m, 2H), 4.35 (d, J = 11.0 Hz, 1H), 3.10 (d, J = 13.7 Hz, 1H), 2.85 (d, J = 13.8 Hz, 1H), 1.46 (s, 18H), 1.28 (s, 9H). 

13C NMR (176 MHz, δ, CDCl3, 298 K): 176.0, 155.0, 153.2, 138.2, 136.6, 134.6, 138.1, 136.7, 135.0, 134.6, 133.4, 131.1, 130.2, 129.0, 128.9, 128.8, 128.6, 128.5, 128.1, 127.8, 125.8, 68.5, 56.4, 55.4, 52.1, 43.3, 34.6, 30.5. 


HPLC (YMC CHIRAL ART Cellulose-SB, eluent: hexane:i-PrOH = 20:1, 0.5 mL/min, 10 °C) retention times: tminor = 30.1 min, tmajor = 22.7 min.

racemic 3s-Cbz

Adduct 3s: (tert-butyl (S)-4-benzyl-4-((S)-(3,5-di-tert-butyl-4-hydroxyphenyl)(4-(trifluoromethyl)phenyl)methyl)-5-oxoisoxazolidine-2-carboxylate): Prepared following the general procedure and obtained as a colorless oil (63.6 mg, 0.099 mmol, 99%, d.r. = 6:1, >99.5% ee). 

Rf (heptanes/EtOAc = 5/1) = 0.50. [α]D23 (c = 0.55, CHCl3) = +74.7°. 

1H NMR (300 MHz, δ, CDCl3, 298 K): 7.52 (d, J = 7.9 Hz, 2H), 7.32 – 7.26 (m, 4H), 7.24 – 7.20 (m, 1H), 7.17 (d, J = 8.0 Hz, 2H), 7.03 (s, 2H), 5.22 (s, 1H), 4.56 – 4.43 (m, 2H), 4.24 (d, J = 10.7 Hz, 1H), 3.13 (d, J = 13.7 Hz, 1H), 2.95 (d, J = 13.7 Hz, 1H), 1.46 (s, 18H), 1.28 (s, 9H), 1.28 (s, 9H). 

13C NMR (75 MHz, δ, CDCl3, 298 K): 176.0, 154.3, 153.2, 139.3, 139.2, 139.2, 136.6, 130.7, 130.1, 129.8, 129.7, 129.1, 128.9, 127.5, 125.9, 125.7, 125.6, 83.7, 56.5, 55.4, 52.1, 42.9, 34.6, 30.5, 28.1. 

19F NMR (282 MHz, δ, CDCl3, 298 K): -62.55 (d, J = 9.4 Hz, 3F). 

HRMS (ESI): calcd m/z for C37H44F3NO5: 657.3510...
[M+NH₄]^+; found: 657.3507. HPLC (YMC CHIRAL ART Cellulose-SB, eluent: hexane:i-PrOH = 200:1, 0.5 mL/min, 10 °C) retention times: tₘᵋᵣᵦ = 23.5 min, tₚᵡᵢᵢᵦ = 20.8 min.

racemic 3t

scalemic 3t

Adduct 3u: (tert-butyl (S)-4-benzyl-4-((S)-(3,5-di-tert-butyl-4-hydroxyphenyl)(naphthalen-2-yl)methyl)-5-oxoisoxazolidine-2-carboxylate): Prepared following the general procedure and obtained as a colorless oil (61.4 mg, 0.099 mmol, 99%, d.r. = 11:1, >99.5% ee). Rᵣ (heptanes/EtOAc = 5/1) = 0.50. [α]ᵡ²³ (c = 0.75, CHCl₃) = +106.2°. ¹H NMR (700 MHz, δ, CDCl₃, 298 K): 8.13 – 8.08 (m, 1H), 7.88 – 7.83 (m, 2H), 7.60 (t, 1H), 7.50 – 7.45 (m, 2H), 7.42 (d, J = 7.2 Hz, 1H), 7.22 – 7.16 (m, 3H), 7.09 (s, 2H), 7.01 – 6.97 (m, 2H), 5.54 (s, 1H), 5.08 (s, 1H), 4.56 (d, J = 10.2 Hz, 1H), 4.51 (d, J = 10.2 Hz, 1H), 3.13 (d, J = 14.0 Hz, 1H), 3.01 (d, J = 14.0 Hz, 1H), 1.32 (s, 18H), 1.31 (s, 9H). ¹³C NMR (176 MHz, δ, CDCl₃, 298 K): 176.5, 154.6, 153.1, 135.8, 135.4, 134.9, 134.7, 132.6, 130.2, 129.1, 128.7, 128.6, 128.1, 127.6, 126.7, 126.0, 125.0, 124.8, 123.9, 83.3, 56.4, 52.5, 50.7, 42.8, 34.5, 30.4, 28.2. HRMS (ESI): calcd m/z for C₄₀H₄₇NO₅: 639.3792 [M+NH₄]^+; found: 639.3794. HPLC (YMC CHIRAL ART Cellulose-SB, eluent: hexane:i-PrOH = 30:1, 0.5 mL/min, 10 °C) retention times: tₘᵋᵦᵦ = 23.5 min, tₚᵡᵢᵦᵦ = 14.4 min.

racemic 3u

scalemic 3u
Adduct 3v (tert-butyl (S)-4-benzyl-4-((S)-(3,5-di-tert-butyl-4-hydroxyphenyl)(pyridin-2-yl)-methyl)-5-oxoisoxazolidine-2-carboxylate): Prepared following the general procedure and obtained as a colorless oil (55.4 mg, 0.097 mmol, 97%, d.r. = 4:1, 96.4% ee). Rf (heptanes/EtOAc = 2/1) = 0.40. [a]D23 (c = 0.80, CHCl3) = +151.3°. 1H NMR (300 MHz, δ, CDCl3, 298 K): 8.56 – 8.50 (m, 1H), 8.50 – 8.42 (m, 1H), 7.79 – 7.69 (m, 1H), 7.30 – 7.26 (m, 2H), 7.25 – 7.21 (m, 2H), 7.07 – 7.02 (m, 4H), 5.25 (s, 1H), 4.45 – 4.30 (m, 3H), 3.11 (d, J = 14.0 Hz, 1H), 2.90 (d, J = 13.7 Hz, 1H), 1.45 (s, 18H), 1.30 (s, 9H). 13C NMR (75 MHz, δ, CDCl3, 298 K): 175.8, 175.6, 154.2, 153.4, 151.2, 148.6, 137.3, 136.8, 135.4, 134.6, 130.3, 128.8, 128.3, 127.9, 126.6, 125.8, 123.6, 83.6, 83.5, 55.1, 54.4, 52.4, 42.9, 42.8, 34.6, 30.4, 30.3, 28.2, 28.1. HRMS (ESI): calcd m/z for C35H44N2O6: 590.3588 [M+NH4]+; found: 590.3591.

HPLC (YMC CHIRAL ART Cellulose-SB, eluent: hexane:i-PrOH = 200:1, 0.5 mL/min, 10 ºC) retention times: tminor = 9.6 min, tmajor = 19.4 min.

racemic 3v (dr. = 2:1) scalemic 3v (dr. = 4:1)

Adduct 3w (tert-butyl (S)-4-benzyl-4-((S,E)-1-(3,5-di-tert-butyl-4-hydroxyphenyl)-3-phenylallyl)-5-oxoisoxazolidine-2-carboxylate): Prepared following the general procedure and obtained as a colorless oil (41.6 mg, 0.070 mmol, 70%, d.r. = 5:1, 98.5% ee). Rf (heptanes/EtOAc = 5/1) = 0.50. [a]D23 (c = 0.65, CHCl3) = +33.5°. 1H NMR (700 MHz, δ, CDCl3, 298 K): 7.38 – 7.36 (m, 2H), 7.31 – 7.27 (m, 4H), 7.26 – 7.22 (m, 2H), 7.13 – 7.11 (m, 2H), 7.04 (s, 2H), 6.62 (dd, J = 15.7, 8.7 Hz, 1H), 6.49 (d, J = 15.6 Hz, 1H), 5.21 (s, 1H), 4.26 (d, J = 10.8 Hz, 1H), 4.02 (d, J = 10.8 Hz, 1H), 3.75 (d, J = 8.8 Hz, 1H), 3.17 (d, J = 13.9 Hz, 1H), 2.67 (d, J = 13.9 Hz, 1H), 1.45 (s, 18H), 1.31 (s, 9H). 13C NMR (176 MHz, δ, CDCl3, 298 K): 175.8, 154.3, 153.4, 137.0, 136.5, 135.1, 134.2, 130.4, 128.8, 128.6, 127.8, 127.6, 127.4, 126.8, 125.3, 83.4, 60.6, 55.1, 55.0, 52.2, 41.6, 34.6, 30.5, 28.2, 28.1. HRMS (ESI): calcd m/z for C38H47NO5: 615.3792.
[M+NH₄]⁺; found: 615.3787. HPLC (YMC CHIRAL ART Cellulose-SB, eluent: hexane:i-PrOH = 200:1, 0.5 mL/min, 10 °C) retention times: t_{minor} = 13.4 min, t_{major} = 22.1 min.

racemic 3w (dr. = 2:1)

scalemic 3w

Adduct 3x (tert-butyl (S)-4-benzyl-4-((S)-1-(3,5-di-tert-butyl-4-hydroxyphenyl)-2,2,2-trifluoroethyl)-5-oxoisoxazolidine-2-carboxylate): Prepared following the general procedure and obtained as a colorless oil (54.9 mg, 0.097 mmol, 97 %). Rf (heptanes/EtOAc = 5/1) = 0.55. [\alpha]_D^{23} (c = 0.95, CHCl₃) = +56.9°. ¹H NMR (700 MHz, δ, CDCl₃, 298 K): 7.26 – 7.23 (m, 3H), 7.03 (s, 2H), 6.99 – 6.93 (m, 2H), 5.37 (s, 1H), 4.64 (d, J = 11.1 Hz, 1H), 4.26 (d, J = 11.1 Hz, 1H), 3.92 (q, J = 9.4 Hz, 1H), 2.82 (d, J = 13.9 Hz, 1H), 2.50 (d, J = 13.9 Hz, 1H), 1.46 (s, 18H), 1.41 (s, 9H). ¹³C NMR (176 MHz, δ, CDCl₃, 298 K): 175.2, 154.7, 154.7, 133.2, 130.5, 128.8, 128.1, 125.9 (q, J = 285 Hz, 1C), 121.1, 83.9, 54.4 (q, J = 25.7 Hz, 1C), 51.7, 50.9, 42.5, 34.5, 30.4, 28.2. ¹⁹F NMR (282 MHz, δ, CDCl₃, 298 K): -63.21 (d, J = 9.4 Hz, 3F). HRMS (ESI): calcd m/z for C₅₁H₆₀F₃NO₅: 851.3197 [M+NH₄]⁺; found: 851.3196. HPLC (YMC CHIRAL ART Cellulose-SB, eluent: hexane:i-PrOH = 300:1, 0.5 mL/min, 10 °C) retention times: t_{minor} = 25.9 min, t_{major} = 46.8 min.

racemic 3x (dr. = 4:1)

scalemic 3x
4. Further Transformations

4.1 Reductive Cleavage of the Isoxazolidin-5-one N-O Bond

Method A:

Under an Argon atmosphere, adduct 3a (1.14 g, 2.00 mmol) and Pd/C (115 mg, 10% w/w) were placed in a round bottom flask and t-BuOH (100 mL) was added. The atmosphere inside the reaction vessel was replaced by H₂ (1 atm) and the mixture was heated to 85 °C. After vigorous stirring for 20 h, the reaction mixture was allowed to cool to room temperature and was subsequently filtered through a pad of Celite®. The solvent was removed in vacuo, giving 4a in sufficient purity (1.12 g, 1.96 mmol, 98%).

Method B:

Under an Argon atmosphere, adduct 3a (57.2 mg, 0.1 mmol), HCO₂NH₄ (63.1 mg, 1 mmol) Pd/C (5.7 mg, 10% w/w) were placed in a round bottom flask and t-BuOH (4 mL) was added. The vigorously stirred suspension was heated to 85 °C and kept at this temperature for 20 h. After completion of the reaction, the mixture was cooled to room temperature and filtered through a pad of Celite®. The solvent was removed in vacuo, giving 4a in sufficient purity (55.7 mg, 0.1 mmol, 97%).

Product 4a ((2S,3S)-2-benzyl-2-(((tert-butoxycarbonyl)amino)methyl)-3-(3,5-di-tert-butyl-4-hydroxyphenyl)-3-phenylpropanoic acid): Prepared following one of the methods described above. Rₓ (heptanes/EtOAc = 2/1) = 0.50. m.p. = 112 – 114 °C. ¹H NMR (300 MHz, δ, CDCl₃, 298 K): 7.51 – 7.43 (m, 2H), 7.30 – 7.27 (m, 1H), 7.26 – 7.14 (m, 7H), 7.12 – 7.06 (m, 2H), 5.13 (s, 1H), 4.56 – 4.20 (m, 2H), 3.58 – 3.40 (m, 2H), 3.29 (d, J = 13.8 Hz, 1H), 2.88 (d, J = 13.9 Hz, 1H), 1.41 (s, 18H), 1.39 (s, 9H). ¹³C NMR (75 MHz, δ, CDCl₃, 298 K): 179.4, 155.9, 153.0, 141.0, 140.9, 136.9, 135.9, 135.8, 130.5, 130.2, 128.3, 128.3, 126.8, 126.8, 79.4, 58.6, 55.4, 43.1, 41.6, 34.5, 30.5, 28.6. HRMS (ESI): calcd m/z for C₃₈H₄₇NO₅: 574.3532 [M+H]+; found: 574.3536.
4.2 Lewis Acid-promoted Debutylation of 4a

Anhydrous AlCl₃ (160.0 mg, 1.2 mmol) was added to a solution of N-Boc protected β-amino acid 4a (114.7 mg, 0.2 mmol) in dry toluene (4 mL) and the mixture was stirred for 2 days at room temperature. After completion of the reaction, the solution was cooled to 0 °C and quenched with water (10 mL). The organic phase was diluted with DCM (15 mL) and extracted with water (15 mL) two times. The aqueous phase was reduced to dryness and the crude residue was subjected to preparative TLC (silica; DCM/MeOH = 5/1) giving debutylated β-amino acid 8a as a colorless powder in 65% yield (47.0 mg, 0.13 mmol).

Product 8a: (2S,3S)-2-(aminomethyl)-2-benzyl-3-(4-hydroxyphenyl)-3-phenylpropanoic acid:

Prepared following the method described above and obtained as a colorless oily solid (47.0 mg, 0.13 mmol, 65%).

Rᵣ (DCM/MeOH = 5/1) = 0.50. ¹H NMR (300 MHz, δ, CD₃OD, 298 K): 7.52 (d, J = 7.6, 2H), 7.27 – 7.17 (m, 10H), 6.77 (d, J = 7.5, 2H), 4.51 (s, 1H), 3.41 – 3.35 (m, 1H), 3.34 – 3.25 (m, 3H), 3.03 (d, J = 13.4, 1H), 2.62 (d, J = 13.3, 1H). ¹³C NMR (75 MHz, δ, CDCl₃, 298 K): 158.2, 144.4, 140.7, 133.5, 132.1, 131.9, 130.4, 129.9, 128.6, 128.1, 117.0, 60.1, 45.2, 30.9, 25.1. HRMS (ESI): calcd m/z for C₂₃H₂₃NO₃: 362.1756 [M+H]+; found: 362.1754.

4.3 KAHA Ligation with N-Fmoc-Leu α-oxo-acid 6

Adduct 3a (57.2 mg, 0.10 mmol) was dissolved in DCM (1 mL) and TFA (0.5 mL) was added. After stirring for 30 min at room temperature, the solvent was removed in vacuo giving a colorless oily residue, which was directly used for the next step. Deprotected 3a was dissolved in t-BuOH/THF/H₂O
(1/1/1; 1.5 mL), 6 (prepared following a reported procedure, 42.0 mg, 0.11 mmol) was added and the mixture was stirred for 20 h at room temperature. After completion of the reaction, water (10 mL) and EtOAc (15 mL) were added and the phases were allowed to separate. The aqueous phase was extracted three times with EtOAc (15 mL), the combined organic phases were dried over Na$_2$SO$_4$, filtered and reduced to dryness in vacuo. 7a was isolated by column chromatography (silica gel, heptanes/EtOAc = 20/1 to 1/1) as a colorless oil (62.3 mg, 0.08 mmol, 77%).

N-protected dipeptide 7a: 

![Chemical Structure](image)

(2S,3S)-2-(((S)-2-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-4-methylpentanamido)methyl)-2-benzyl-3-(3,5-dimethyl-3-phenylpropanoic acid): Obtained as a colorless oil (62.3 mg, 0.08 mmol, 77%). R$_f$ (heptanes/EtOAc = 2/1) = 0.45. $^1$H NMR (300 MHz, CDCl$_3$, 298 K): 7.78 – 7.73 (m, 2H), 7.57 (t, $J$ = 8.0 Hz, 2H), 7.49 – 7.34 (m, 6H), 7.31 – 7.28 (m, 1H), 7.24 – 7.18 (m, 5H), 7.10 – 7.07 (m, 4H), 6.01 – 5.89 (m, 1H), 5.14 (s, 1H), 4.84 (d, $J$ = 8.8 Hz, 1H), 4.45 – 4.42 (m, 1H), 4.38 – 4.34 (m, 1H), 4.19 – 4.15 (m, 1H), 3.80 – 3.75 (m, 1H), 3.68 – 3.61 (m, 1H), 3.37 (d, $J$ = 13.8 Hz, 1H), 2.81 (d, $J$ = 13.7 Hz, 1H), 1.46 – 1.39 (m, 21H), 0.89 (s, 3H), 0.82 (s, 3H). $^{13}$C NMR (75 MHz, CDCl$_3$, 298 K): 171.9, 152.9, 144.1, 143.8, 141.5, 141.4, 140.8, 137.9, 135.8, 130.4, 130.1, 128.4, 127.9, 127.2, 126.9, 126.8, 125.2, 120.1, 67.0, 60.6, 58.8, 55.1, 53.5, 47.3, 42.9, 41.6, 41.5, 34.5, 30.5, 24.7, 23.2. HRMS (ESI): calcd m/z for C$_{52}$H$_{60}$N$_2$O$_6$: 809.4530 [M+H]$^+$; found: 809.4527.

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5. Copies of NMR Spectra of New Compounds

![NMR Spectra of New Compounds]
$\text{O} \text{N-} \text{Boc}$

$1n$

$\text{O} \text{N-} \text{Boc}$

$1m$
3q

3r