**Brønsted Acid-Catalyzed Epimerization-Free Preparation of Dual-Protected Amino Acid Derivatives**

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*Supporting Information

**ABSTRACT:** An organocatalytic protocol, employing the commercially available EDC as coupling agent, has been developed for the preparation of dual-protected amino acid derivatives without epimerization. This methodology was then applied to different Boc-amino acid and amine derivatives in moderate to excellent isolated yields. In addition, racemization-free Boc deprotection was also demonstrated. Mechanism investigation through electrospray ionization (+)-mass spectrometry/mass spectrometry revealed an acyclic intermediate (no azlactone formation) activated by the camphorsulfonic acid as an organocatalyst as a key step for the sequential attack of the nucleophile.

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**RESULTS AND DISCUSSION**

In our attempt to prepare 2-alcoxy-oxazolone derivatives, N-Boc-amino acids were chosen as substrates. Initially, L-isoleucine, which contains 2 stereocenters, and therefore the epimerization of the α-carbonyl hydrogen would result in a pair of diastereomers, was chosen as an ideal substrate. This, in fact, would allow us to observe racemization from the crude reaction mixture 

During the reaction of N-Boc-L-isoleucine with EDC, the formation of an unstable intermediate was observed by thin-layer chromatography (TLC). Due to this instability, the crude reaction mixture was washed with distilled cold water three times, and the dichloromethane immediately employed, forming an unstable intermediate was observed by thin-layer chromatography (TLC). Due to this instability, the crude reaction mixture was washed with distilled cold water three times, and the dichloromethane immediately employed, without further purification, in a sequential reaction in the presence of pyrrolidine as nucleophile. To our delight, the desired product was isolated in 38% yield and without apparent epimerization. After new attempts to increase the general yields, it was found that the use of 10 mol % of (±)-camphorsulfonic acid (CSA) as organocatalyst resulted in an increase to 73% yield.

Having established this catalytic system for the epimerization-free formation of the amino acid amide derivative, we proceeded to test the generality of these reaction conditions with a range of different Boc-amino acids and amines. Initially,
primary aliphatic and aromatic amines were examined, providing products 2a−p in yields ranging from 52 to 81% (Scheme 2). Anilines also worked well, providing 2m and 2n in 73−76% yields. Even the use of ortho-substituted aniline was well tolerated, affording 2o in 70% yield. The heteroaromatic 2-amino-3-picoline proved to be reactive under the developed reaction conditions, providing 2p in a 52% isolated yield.

Next, we turned our attention toward the secondary amines as nucleophiles. Compounds 2q−ag were isolated in yields ranging from 61 to 86% (Scheme 3), with no need of purification by the chromatographic column. Different Boc-amino acids could also be employed, with no significant influence on the reaction yield.

It is worth mentioning that no epimerization was observed by NMR for any of i-isoleucine derivatives. The relative and absolute stereochemistry of the compound 2m was determined by the X-ray crystallographic structure (Figure 1A), with maintenance of the original (2S,3S)-isoleucine stereocenters. Compound 2x and its racemic mixture 2y, prepared using D,L-alanine were also evaluated by chiral high-performance liquid chromatography (HPLC) (Figure 1B), providing another insight into the epimerization-free nature of this transformation.

We also decided to investigate the racemization process during Boc deprotection. Employing classical reaction conditions,31 products 2ac and 2q in the presence of TFA afforded the desired salts 2ag and 2ah in 86 and 84% yield (Scheme 4).

We then turned our attention toward the understanding of the basics of this reaction by investigating the plausible key intermediate. To this end, two experiments were carried out in triplicate employing Boc-i-isoleucine and EDC. First, a crude reaction mixture was transferred to the gas phase by electrospray ionization (ESI), followed by (tandem) mass spectrometry (MS) characterization ESI(+)-MS/MS. The other experiment consisted of analyzing the same sample after the dichloromethane was washed with distilled water (for the removal of EDC and its urea) and dried under reduced pressure. Surprisingly, both samples showed no sign of an azlactone intermediate; however, an ion of m/z 387.2971 was

Scheme 1. Previous Reports on Epimerization-Free Preparation of Amino Acid Amides

(A) Hu, 2016

(B) Dev, 2014

(C) Dunetz, 2011

(D) Our proposal
found in both experiments and was extremely abundant in the purified sample (see Supporting Information).

This key species of m/z 387 corresponds to intermediate 1 (Figure 2), the Boc-L-isoleucine activated by EDC. We propose that due to a torsional problem, different from Fmoc or Cbz-amino acids with previously reported X-ray crystallographic structures, the tert-butoxy group prevents the intramolecular cyclization and azlactone formation. Moreover, because the pK_a of an α-carbonyl hydrogen of an azlactone is considerably lower than that of an acyclic amino acid, this helps to explain the epimerization-free nature of this reaction.

Finally, the organocatalytic mechanism was investigated by ESI(+)-MS/MS. For this purpose, the previous crude reaction sample bearing ion m/z 387 was added to 10 mol % of the CSA catalyst and immediately injected into the mass spectrometer. Two ions of m/z 641.3555 and of m/z 657.3298 corresponding to the association of the intermediate 1 and the catalyst, that is, [M + Na]^+ and [M + K]^+ were intercepted (Figure 3A). The collision-induced dissociation of m/z 641 shows fragment ions of m/z 387 and 409 (Figure 3B), corresponding to the intermediate 1 [M + H]^+ and [M + Na]^+, due to the neutral loss of CSA. Therefore, as previously reported for other Brønsted acid catalysts, the mechanism seems to proceed through an ion-pairing intermediate that is then followed by amine nucleophilic attack.

Scheme 2. Epimerization-Free Preparation of Amino Acid Amides Employing Primary Amines as Nucleophiles

Scheme 3. Epimerization-Free Preparation of Amino Acid Amides Employing Secondary Amines as Nucleophiles

Compounds 2s and 2y are, respectively, the racemic mixtures of 2r and 2x. Reaction also carried out on a gram scale.
CONCLUSIONS

In summary, general conditions have been reported for the organocatalytic and epimerization-free preparation of dual-protected amino acid derivatives under mild reaction conditions. A broad substrate scope has been presented, allowing changes in the amino acid and the amine nucleophile, proving the generality of this protocol. Boc deprotection was also carried out in excellent yields and without racemization. ESI(+)−MS/MS experiments revealed an acyclic intermediate, unlike azlactone formation. Finally, the organocatalytic mechanism investigation revealed intermediate activation by the catalyst CSA to form an ion-pairing intermediate, that is then followed by nucleophilic attack.

EXPERIMENTAL SECTION

General Methods. All purchased chemicals were used as received without further purification. Solvents were dried according to standard procedures. Analytical TLC was performed on TLC plates (silica gel 60 F254) and visualized employing a ninhydrin (2,2-dihydroxyindane-1,3-dione) in-

Figure 1. A) X-ray crystallographic structure of 2m (anisotropic displacement ellipsoids are drawn at the 50% probability level) (B) Chiral HPLC of 2x and its racemic mixture, 2y.

Scheme 4. Epimerization-Free Boc Deprotection of Compounds 2q and 2ac

Figure 2. ESI(+)−MS of crude reaction between Boc-L-isoleucine and EDC.
The chemical shifts are reported in ppm relative to the solvent residual peak. The $^1$H NMR spectra were recorded at 500 MHz, $^{13}$C NMR spectra were recorded at 125 MHz. Chemical shifts are reported in ppm using the following peak pattern abbreviations: br, broad; s, singlet; d, doublet; t, triplet; q, quartet; pent, pentet; sext, sextet; m, multiplet. High-resolution mass spectra, as well as mechanism investigation were investigated in the positive ion mode using a time-of-flight (TOF) mass spectrometer equipped with an ESI source or a matrix-assisted laser desorption (MALDI)/TOF spectrometer using a pulsed nitrogen laser at 337 nm. Single-crystal data for compound 2m were collected with a diffractometer with Mo Ka ($\lambda = 0.71073$ Å) radiation at room temperature (298 K). The data collection, cell refinements, and data reduction were performed using the CRYSALISPRO software. To elucidate the structure, an empirical absorption correction using the faces’ crystal model was employed. The structures were resolved by direct methods and refined by full-matrix least square refinement on F2 using the SHELXL-2014 program package, and all nonhydrogen atoms were refined with anisotropic thermal parameters. H atoms connected to carbon were placed in idealized positions and treated by the rigid model, with Uiso(H) = 1.2 Ueq(C) for the aromatic ring and Uiso(H) = 1.5 Ueq(C) for methyl groups. CCDC 1539443 has the supplementary crystallographic data for this work, and it can be obtained free of charge from the Cambridge Crystallographic Data Centre at http://www.ccdc.cam.ac.uk/contents/retrieving.html. The figures were drawn using ORTEP-3 for Windows and Mercury programs. Enantiodiscriminating HPLC was performed using a 4.6 × 25 cm$^2$ Chiralpak IA column (isocratic elution using hexane/isopropanol 88:12; flow 0.5 mL/min). Melting points and optical rotations were recorded, respectively, on a melting point apparatus and a polarimeter.

**General Method: Organocatalyzed Preparation of Amino Acids Amides.** In a round-bottom flask, N-Boc-amino acid (i.e., L-alanine, L-phenylalanine, L-valine, L-leucine, or L-isoleucine) (1.0 mmol) and EDC $\cdot$ HCl (211 mg, 1.1 mmol) were dissolved in dichloromethane (15.0 mL), and the reaction was stirred at 0 °C for 30 min. The crude reaction was washed with distilled water three times, and the dichloromethane immediately employed, without further purification. This solution was then transferred to a round-bottom flask containing the amine nucleophile (2.0 mmol) and the ($\pm$)-camphorsulfonic acid (23 mg, 10 mol %). After 24 h, the reaction was concentrated in vacuo, and for L-isoleucine derivatives, an aliquot was taken to the NMR spectrometer for analysis of the epimerization by $^1$H NMR analysis. The desired products were then purified by recrystallization in hot EtOH/water, liquid–liquid extraction, or column chromatography.

**General Method: Boc Deprotection of Amino Acids Amides.** In a round-bottom flask, Boc-L-amino acid amide (1.0 mmol, 1.0 equiv) was dissolved in anhydrous CH$_2$Cl$_2$ (10 mL),...
and TFA (1 mL, 22.0 equiv) was added. After 3 h stirring at room temperature, the reaction was concentrated in vacuo, directly affording the unprotected product as a yellow/orange oil.

tert-Butyl (25S,35S)-1-(Hexylamino)-3-methyl-1-oxopentan-2-ylcarbamate (2a). The product was prepared according to the general procedure and obtained after recrystallization in ethanol/water as a white solid (246 mg, 78%). Mp: 80, 4–81, 6 °C. [α]D20 = −14° (c = 1.0, CH2Cl2). Fourier transform infrared (FT-IR) (diamond) ν 3334, 3308, 2963, 2925, 2880, 2864, 1679, 1655, 1524, 1168 cm−1. 1H NMR (500 MHz, CDCl3) δ 6.02 (br, 1H), 5.09 (br, 1H), 3.86 (dd, J = 8.85, 6.75 Hz, 1H), 3.30–3.17 (m, 2H), 1.85 (br, 1H), 1.50–1.47 (m, 2H), 1.43 (s, 9H), 1.29–1.24 (m, 7H), 1.14–1.05 (m, 1H), 0.91–0.86 (m, 9H). 13C NMR (125 MHz, CDCl3) δ 171.6, 156.0, 79.9, 59.6, 39.6, 37.2, 31.6, 29.6, 28.5, 26.7, 24.9, 22.7, 15.7, 14.1, 11.5. High-resolution mass spectrometry (HRMS) (ESI-TOF) m/z: [M + Na]+ calcd for C25H50N2O3Na+ 449.3719, found 449.3717.

tert-Butyl (25S,35S)-1-(Aminopropylamino)-3-methyl-1-oxopentan-2-ylcarbamate (2f). The product was prepared according to the general procedure and obtained after liquid–liquid extraction in dichloromethane/water as a yellow oil (231 mg, 67%). [α]D20 = −12° (c = 1.0, CH2Cl2). FT-IR (diamond) ν 3340, 2971, 2918, 2866, 1767, 1656, 1519, 1244, 1172 cm−1.

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tert-Butyl (S)-(1-(Benzylinolo)-1-oxo-3-phenylpropan-2-yl)carbamate (2j). The product was prepared according to the general procedure and obtained after recrystallization with ethanol/water as a white solid (388 mg, 73%). Mp: 126, 7–127, 6 °C. [α]20 = +72° (c = 1.0, CHCl3). FT-IR (KBr) ν 3340, 3028, 2972, 2922, 1692, 1662, 1526, 1173 cm⁻¹. 1H NMR (500 MHz, CDCl3) δ 7.29–7.72 (m, 2H), 7.18 (d, J = 6.85 Hz, 2H), 7.09 (d, J = 5.45 Hz, 2H), 6.15 (br, 1H), 5.09 (br, 1H), 4.34 (d, J = 5.55 Hz, 3H), 3.12–3.03 (m, 2H), 1.39 (s, 9H). 13C NMR (125 MHz, CDCl3) δ 171.3, 155.6, 137.9, 136.9, 129.6, 128.8, 127.9, 127.7, 121.4, 80.4, 56.3, 43.7, 38.8, 24.4. HRMS (MALDI-TOF) m/z: [M + H]+ calcld for C16H31N2O3 279.1703, found 279.1678.

tert-Butyl (S)-(1-(Benzylinolo)-4-methyl-1-oxopentan-2-yl)carbamate (2k). The product was prepared according to the general procedure and obtained after recrystallization with ethanol/water as a white solid (379 mg, 79%). Mp: 76, 5–157, 6 °C. [α]20 = +88° (c = 1.0, CHCl3). FT-IR (KBr) ν 3428, 3302, 3098, 3058, 2960, 2930, 2867, 1692, 1662, 1527, 1173 cm⁻¹. H NMR (500 MHz, CDCl3) δ 7.26–7.25 (m, 2H), 7.21–7.19 (m, 3H), 7.13 (br, 1H), 5.29 (d, J = 7.30 Hz, 1H), 4.41–4.37 (m, 1H), 4.32–4.28 (m, 3H), 4.20 (m, 1H), 1.66–1.60 (m, 2H), 1.53–1.47 (m, 1H), 1.37 (s, 9H), 0.91–0.88 (m, 6H). 13C NMR (125 MHz, CDCl3) δ 173.0, 165.0, 138.4, 128.7, 127.6, 127.4, 79.9, 53.2, 43.4, 41.4, 28.4, 24.8, 23.0, 22.1. HRMS (MALDI-TOF) m/z: [M + H]+ calcld for C16H29N2O3 355.1606, found 355.1989.

tert-Butyl (S)-(1-(Benzylinolo)-3-methyl-1-oxobutan-2-yl)carbamate (2l). The product was prepared according to the general procedure and obtained after recrystallization with ethanol/water as a white solid (326 mg, 70%). Mp: 110, 5–151, 3 °C. [α]20 = +18° (c = 1.0, CHCl3). FT-IR (KBr) ν 3302, 2966, 2929, 2879, 1700, 1652, 1426, 1200, 1167 cm⁻¹. 1H NMR (500 MHz, CDCl3) δ 8.33 (dd, J = 8.00 Hz, 1H), 8.26 (br, 1H), 7.03 (t, J = 7.80 Hz, 1H), 6.97 (t, J = 7.60 Hz, 1H), 6.85 (t, J = 8.00 Hz, 1H), 5.22 (d, J = 6.85 Hz, 1H), 4.15 (br, 1H), 3.84 (s, 3H), 1.98 (br, 1H), 1.57–1.53 (m, 1H), 1.45 (s, 9H), 1.25–1.15 (m, 1H), 0.98 (d, J = 6.30 Hz, 3H), 0.92 (t, J = 7.40 Hz, 3H). 13C NMR (125 MHz, CDCl3) δ 169.9, 155.9, 148.2, 127.3, 124.1, 121.1, 119.9, 110.1, 80.0, 52.5, 37.6, 28.4, 24.9, 15.7, 11.6. HRMS (ESI-TOF) m/z: [M + Na]+ calcld for C17H33N2O3Na+ 359.1941, found 359.1948.

tert-Butyl (2S,3S)-1-((2-Methylpyridin-3-yl)-aminol)-1-oxopentan-2-yl)carbamate (2p). The product was prepared according to the general procedure and obtained after recrystallization with ethanol/water as a green oil (167 mg, 52%). [α]20 = +8° (c = 1.0, CHCl3). FT-IR (KBr) ν 3268, 3010, 2971, 2929, 1678, 1524, 1173, 747 cm⁻¹. 1H NMR (500 MHz, CDCl3) δ 8.89 (br, 1H), 8.26 (d, J = 4.65 Hz, 1H), 7.53 (d, J = 6.70 Hz, 1H), 7.10–7.07 (m, 1H), 5.34–5.32 (m, 1H), 4.24 (br, 1H), 2.24 (s, 3H), 1.99–1.97 (m, 1H), 1.61–1.55 (m, 1H), 1.43 (s, 9H), 1.20–1.14 (m, 1H), 1.00 (d, J = 6.80 Hz, 3H), 0.90 (t, J = 7.40 Hz, 3H). 13C NMR (125 MHz, CDCl3) δ 170.9, 161.4, 156.2, 149.3, 145.9, 140.1, 121.9, 80.2, 59.8, 37.3, 28.5, 24.8, 18.4, 15.9, 11.6. HRMS (MALDI-TOF) m/z: [M + H]+ calcld for C17H31N2O3Na+ 322.2125, found 322.2096.

tert-Butyl (2S,3S)-1-((Diethylamino)-3-methyl-1-oxopentan-2-yl)carbamate (2q). The product was prepared according to the general procedure and obtained after liquid–liquid extraction in dichloromethane/water as a yellow oil (1031 mg, 72%). [α]20 = −6° (c = 1.0, CHCl3). FT-IR (diamond) ν 3299, 2968, 2933, 2875, 1704, 1633, 1168 cm⁻¹. 1H NMR (500 MHz, CDCl3) δ 5.17 (d, J = 9.40 Hz, 1H), 4.33 (t, J = 8.25 Hz, 1H), 3.58–3.51 (m, 1H), 3.44–3.29 (m, 2H), 3.14–3.08 (m, 1H), 1.64–1.62 (m, 1H), 1.52–1.49 (m, 2H), 1.36 (s, 9H), 1.16 (t, J = 7.00 Hz, 1H), 1.06 (t, J = 7.00 Hz, 1H), 0.85–0.81 (m, 6H). 13C NMR (125 MHz, CDCl3) δ 171.7, 155.7, 79.3, 54.3, 42.1, 40.3, 38.6, 28.4, 24.2, 15.7, 14.6, 12.9, 11.4. HRMS (ESI-TOF) m/z: [M + Na]+ calcld for C17H33N2O3Na+ 309.2149, found 309.2155.

tert-Butyl (S)-(1-(Diethylamino)-1-oxopropan-2-yl)carbamate (2r). The product was prepared according to the general procedure and obtained after liquid–liquid extraction in dichloromethane/water as a yellow oil (164 mg, 61%). [α]20 =
tart-Butyl (1-Diethylamino)-1-oxopropan-2-ylcarbamate (2S). The product was prepared according to the general procedure and obtained after liquid–liquid extraction in dichloromethane/water as a yellow solid (322 mg, 79%). $[^1]C NMR (125 MHz, CDCl$_3$): $\delta$ 171.5, 155.9, 79.4, 55.5, 42.1, 40.3, 32.2, 28.4, 19.7, 17.6, 14.7, 13.0. HRMS (MALDI-TOF) $m/z$: [M + Na]$^+$ calc for C$_{12}$H$_{22}$N$_2$O$_4$Na$^+$ 267.1679, found 267.1684.

tart-Butyl (S)-(1-Diethylamino)-3-methyl-1-oxobutan-2-ylcarbamate (2T). The product was prepared according to the general procedure and obtained after liquid–liquid extraction in dichloromethane/water as a yellow oil (322 mg, 79%). $[^1]C NMR (125 MHz, CDCl$_3$): $\delta$ 171.6, 155.9, 79.4, 55.5, 42.1, 40.3, 32.2, 28.4, 19.7, 17.6, 14.7, 13.0. HRMS (MALDI-TOF) $m/z$: [M + Na]$^+$ calc for C$_{12}$H$_{22}$N$_2$O$_4$Na$^+$ 267.1679, found 267.1684.

tart-Butyl (S)-(1-Diethylamino)-4-methyl-1-oxopentan-2-ylcarbamate (2U). The product was prepared according to the general procedure and obtained after liquid–liquid extraction in dichloromethane/water as a yellow oil (322 mg, 79%). $[^1]C NMR (125 MHz, CDCl$_3$): $\delta$ 171.5, 155.9, 79.4, 55.5, 42.1, 40.3, 32.2, 28.4, 19.7, 17.6, 14.7, 13.0. HRMS (MALDI-TOF) $m/z$: [M + Na]$^+$ calc for C$_{12}$H$_{22}$N$_2$O$_4$Na$^+$ 281.1472, found 281.1477.

tart-Butyl (S)-(3-Methyl-1-morpholin-1-oxopentan-2-yl)carbamate (2V). The product was prepared according to the general procedure and obtained after liquid–liquid extraction in dichloromethane/water as a yellow oil (322 mg, 79%). $[^1]C NMR (125 MHz, CDCl$_3$): $\delta$ 171.5, 155.9, 79.4, 55.5, 42.1, 40.3, 32.2, 28.4, 19.7, 17.6, 14.7, 13.0. HRMS (MALDI-TOF) $m/z$: [M + Na]$^+$ calc for C$_{12}$H$_{22}$N$_2$O$_4$Na$^+$ 287.1965, found 287.1992.

tart-Butyl (S)-(4-Methyl-1-morpholin-1-oxo-3-phenylpropan-2-yl)carbamate (2W). The product was prepared according to the general procedure and obtained after liquid–liquid extraction in dichloromethane/water as a yellow oil (322 mg, 79%). $[^1]C NMR (125 MHz, CDCl$_3$): $\delta$ 171.5, 155.9, 79.4, 55.5, 42.1, 40.3, 32.2, 28.4, 19.7, 17.6, 14.7, 13.0. HRMS (MALDI-TOF) $m/z$: [M + Na]$^+$ calc for C$_{12}$H$_{22}$N$_2$O$_4$Na$^+$ 301.2122, found 301.2097.
general procedure and obtained after liquid–liquid extraction in dichloromethane/water as a yellow oil (381 mg, 76%). \([\alpha]_D^{20} = +22^\circ (c = 1.0, CH_2Cl_2). FT-IR (KBr) \nu 3436, 3313, 3032, 2975, 2916, 2859, 1722, 1649, 1457, 1178 cm^{-1}. 1^H NMR (500 MHz, CDCl_3) \delta 7.29–7.19 (m, 5H), 5.53 (dd, J = 8.50 Hz, 1H), 4.81–4.47 (m, 1H), 3.59–3.53 (m, 2H), 3.49–3.39 (m, 2H), 2.95–2.85 (m, 4H), 1.41 (s, 9H). 13C NMR (125 MHz, CDCl_3) \delta 170.4, 155.2, 136.5, 129.6, 129.5, 128.8, 128.5, 128.7, 127.2, 79.9, 66.5, 66.1, 50.9, 46.1, 42.3, 40.5, 28.4. HRMS (MALDI-TOF) m/z: [M + H]^+ calcd for C_{12}H_{22}N_2O_3 335.1965, found 335.1935.

tert-Butyl (25S,35S)-3-Methyl-1-oxo-1-(pyrrolidin-1-yl)pentan-2-yl)carbamate (Zac). The product was prepared according to the general procedure and obtained after liquid–liquid extraction in dichloromethane/water as a yellow oil (391 mg, 73%). \([\alpha]_D^{20} = +8^\circ (c = 1.0, CH_2Cl_2). FT-IR (diamond) \nu 3285, 2967, 2867, 1704, 1634, 1163 cm^{-1}. 1^H NMR (500 MHz, CDCl_3) \delta 5.22 (d, J = 9.35 Hz, 1H), 4.21 (dd, J = 9.30, 7.45 Hz, 1H), 3.68–3.63 (m, 1H), 3.50–3.34 (m, 3H), 1.93–1.88 (m, 2H), 1.85–1.78 (m, 2H), 1.68–1.62 (m, 1H), 1.55–1.50 (m, 1H), 1.37 (s, 9H), 1.11–1.03 (m, 1H), 0.87 (d, J = 6.80 Hz, 3H), 0.83 (t, J = 7.45 Hz, 3H). 13C NMR (125 MHz, CDCl_3) \delta 171.0, 155.8, 79.4, 56.4, 46.8, 45.8, 38.0, 28.4, 26.1, 24.3, 15.6, 11.3. HRMS (MALDI-TOF) m/z: [M + H]^+ calcd for C_{15}H_{29}N_2O_3 3435, 3313, 3032, 2976, 2946, 2885, 1650, 1201, 1141, 752 cm^{-1}. 1^H NMR (500 MHz, CDCl_3) \delta 143.0 (br, 1H), 8.07 (s, 2H), 4.18 (s, 1H), 3.58–3.51 (m, 1H), 3.40–3.32 (m, 1H), 3.26–3.19 (m, 1H), 3.14–3.07 (m, 1H), 1.86–1.85 (m, 1H), 1.54–1.50 (m, 1H), 1.24–1.18 (m, 1H), 1.14 (t, J = 7.10 Hz, 3H), 1.04 (t, J = 6.95 Hz, 3H), 1.00 (d, J = 6.95 Hz, 3H), 0.86 (t, J = 7.25 Hz, 3H). 13C NMR (125 MHz, CDCl_3) \delta 167.8, 161.2, 115.9 (q, J = 287.5 Hz, CF_3), 55.5, 42.5, 40.9, 36.9, 23.6, 15.1, 13.7, 12.4, 11.4. HRMS (MALDI-TOF) m/z: [M + H]^+ calcd for C_{15}H_{29}N_2O_3 3436, 3314, 3032, 2976, 2946, 2885, 1650, 1201, 1141, 752 cm^{-1}.

**Notes**

*1*H NMR (500 MHz, CDCl_3) \nu 170.1, 155.2, 136.7, 129.5, 128.4, 126.9, 79.6, 53.7, 46.3, 45.7, 40.2, 28.4, 25.8, 24.1. HRMS (MALDI-TOF) m/z: [M + H]^+ calcd for C_{15}H_{29}N_2O_3 3436, 3314, 3032, 2976, 2946, 2885, 1650, 1201, 1141, 752 cm^{-1}.

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