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Total Synthesis of the Cyclopeptide Alkaloid Abyssenine A. Application of Inter- and Intramolecular Copper-Mediated Coupling Reactions in Organic Synthesis

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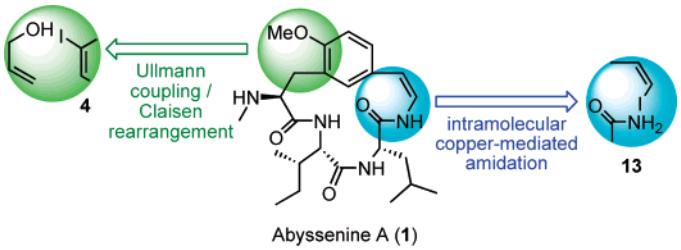

The first total synthesis of the 15-membered ring cyclopeptide alkaloid abyssenine A **1** has been achieved with a longest linear sequence of 15 steps. Central to the synthetic approach was an efficient copper-mediated Ullmann coupling/Claisen rearrangement sequence allowing for both ipso and ortho functionalization of aromatic iodide **4**. This sequence was used for the synthesis of the aromatic core. The synthetic utility of copper-catalyzed coupling reactions was further demonstrated to install the enamide with a concomitant straightforward macrocyclization starting from acyclic α-amido-ω-vinyl iodide **13**.

Introduction

Copper-catalyzed C−N and C−O bond formation has long been a practical and efficient method for the construction of aromatic amides and ethers. Recently, improved versions of these Ullmann and Goldberg coupling reactions relying on the use of new ligands for the stabilization of the active copper species led to considerable improvements of the original procedures,[1] allowing for the use of a wide range of substrates and mild reaction conditions[2,3] together with the extension of these coupling reactions to the use of vinyl halides for the synthesis of enamides[4] and enol ethers.[5] However, whereas the development of new catalytic systems has received considerable attention over the past decade, applications of these procedures for the synthesis of complex molecules remain relatively undeveloped even if they clearly allow for new and efficient bond disconnections, as demonstrated by their use for the installation of key-structural elements of complex natural products.[6,7]

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More recently, intramolecular versions of these copper-catalyzed coupling reactions have been reported by Panek,[8] Li,[9] Ma,[10] and us[11] and used as challenging but efficient macrocyclization procedures.[12] In this contribution, we report on the use of an intramolecular copper-mediated macroamidation reaction, culminating in the first total synthesis of abyssenine A **1** (Figure 1).

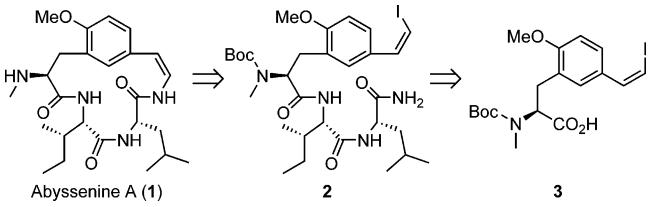

FIGURE 1. Retrosynthetic analysis of abyssenine A (**1**).

This 15-membered ring macrocycle, isolated from the roots and stem bark of several *Zizyphus*-type Rhamnaceae,[13] is part of the cyclopeptide alkaloids class of natural products, a family that encompasses over two hundred compounds and has been shown to display numerous biological activities including sedative, antibacterial, antifungal, and antiplasmodial.[14] While much work has been devoted to the synthesis of the 13- or 14-membered ring cyclopeptide alkaloids,[11,15] a single synthesis of a 15-membered ring compound, mucronine B, featuring a macrolactamization reaction and a stepwise installation of the enamide, has been reported to date.[16] We therefore report in this paper the total synthesis of abyssenine A **1** using copper-mediated coupling reactions for the installation of key-structural elements.

Results and Discussion

Retrosynthetic Analysis. Our strategy for the synthesis of abyssenine A **1** is outlined in Figure 1. Facile generation of the fully elaborated macrocyclic core relies on a challenging copper-mediated intramolecular amidation reaction using amido-vinyl iodide **2** as the enamide precursor. The synthesis of this acyclic intermediate **2** would then just require an efficient preparation of the highly functionalized, suitably protected, amino acid **3**.

Synthesis of the Amino Acid Fragment 3. The amino acid fragment **3** was constructed as shown in Scheme 1. Exposure of a mixture of aromatic iodide **4** and allyl alcohol to catalytic amounts of copper iodide and 1,10-phenanthroline followed by simply heating the intermediate allyl ether to 240 °C allowed for a clean and efficient intermolecular Ullmann coupling−Claisen rearrangement sequence giving trisubstituted phenol **5** in excellent yield. Subsequent isomerization of the double bond with catalytic amounts of $RuClH(CO)(PPh_3)_3$ cleanly gave conjugated alkene **6** which was next methylated before being subjected to oxidative cleavage to give aldehyde **7**, a compound that could hardly be obtained using standard aromatic chemistry techniques.[17] Horner−Emmons reaction of **7** with phosphonate **8**[18] gave the (*Z*)-dehydrophenylalanine derivative **9** and set the stage for the enantioselective installation of the amino acid moiety. Catalytic asymmetric hydrogenation of **9** proceeded smoothly in the presence of $[Rh(COD)\{(S,S)\text{-Et-DuPHOS}\}]^+$-$TfO^-$[19] to afford the corresponding amino ester **10** with good yield and enantioselectivity (89%, 98% ee), the latter being finally methylated under racemization-free conditions.[20] To install the *Z*-vinyl iodide required for the final macroamidation step, the TBS ether was deprotected using TBAF in THF, and the resulting primary alcohol was oxidized to **11** with Dess−Martin periodinane in good overall yield. Finally, Wittig olefination using the Stork/Zhao protocol[21] followed by careful saponification of the methyl ester led to the desired amino acid fragment **3** as (*Z*)-diastereoisomer exclusively.

Assembly of the Acyclic Skeleton. Having in hand useful quantities of the amino acid fragment **3**, the assembly of the acyclic skeleton of abyssenine A was next undertaken. To avoid a stepwise installation of the amide group required for the macrocyclization step after introduction of the other two constitutive amino acids of the macrocycle, a direct peptide bond formation between **3** and isoleucine-leucinamide **12**[22] was envisioned. This quite simple fragment coupling proved to be especially challenging, but after screening a variety of coupling

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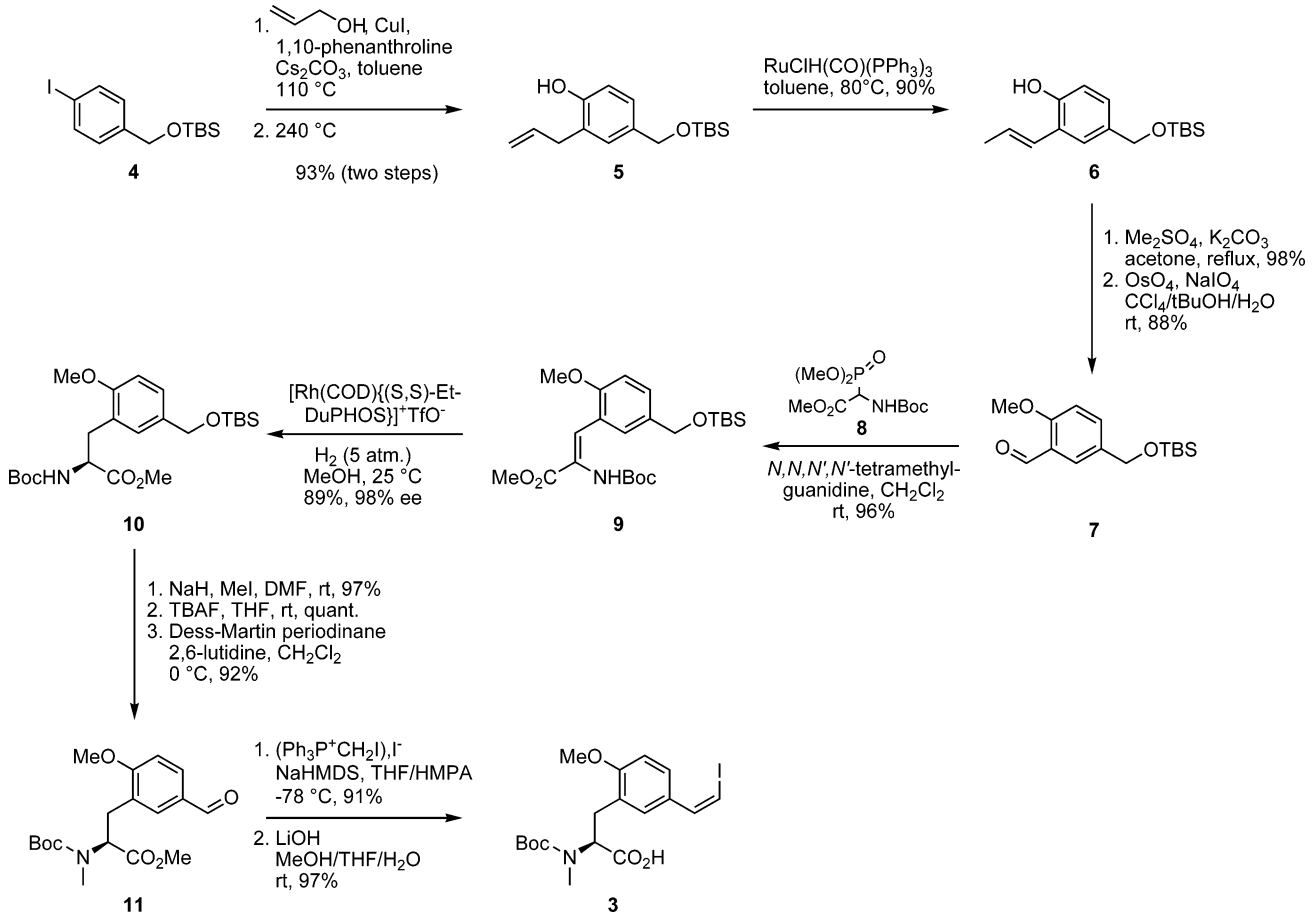
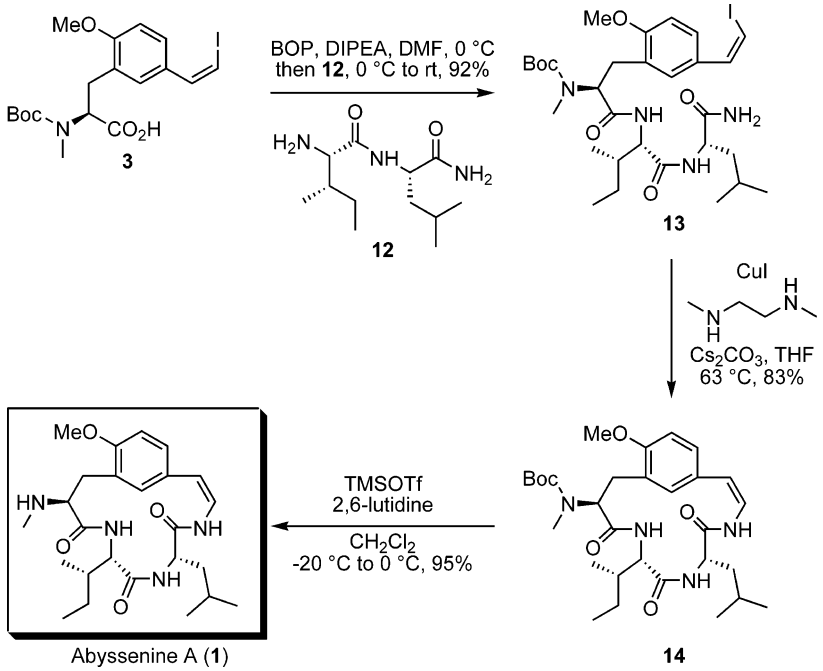
SCHEME 1. Enantioselective Synthesis of the Amino Acid Fragment



SCHEME 2. Macrocyclization and Completion of the Synthesis



agents and conditions, we eventually found that activation of **3** with BOP and further reaction with **12** gave the fully elaborated acyclic skeleton **13** in excellent yield and without any noticeable epimerization (Scheme 2).

Macrocyclization and Completion of the Synthesis. This set the stage for the crucial macrocyclization step:[11] subjection of the iodo-amide **13** to catalytic copper(I) iodide and *N*,*N*′-dimethylethylenediamine[4b] in THF under high dilution condi-

tions at 63 °C smoothly provided the 15-membered ring **14** in 83% yield. The most striking feature of this approach is that this mild intramolecular amidation protocol proceeds with complete regioselectivity for the terminal amide, without any epimerization at the three amino acid stereocenters or isomerization of the *Z* vinyl iodide and without dimerization or formation of higher oligomers. Finally, careful removal of the Boc group using TMSOTf and 2,6-lutidine provided synthetic abyssenine A **1** which was identical in all respects (^{1}H NMR, ^{13}C NMR, $[\alpha]_D^{20}$, IR, UV, and MS) to the natural product, therefore establishing both its relative and absolute configurations.

In summary, the first total synthesis of abyssenine A has been achieved in 15 steps (longest linear sequence) and excellent overall yield (35%). Notable features of our synthetic approach include an original and efficient copper(I)-catalyzed Ullmann coupling/Claisen rearrangement sequence which allows for both *ipso* and *ortho* functionalization of an aromatic iodide. This effort also documents an efficient intramolecular copper(I)-mediated vinylation protocol to install the 15-membered macrocyclic enamide. This should contribute to further expand the scope of those underdeveloped useful reactions which clearly allow for new bond disconnections in total synthesis and should permit for the preparation of other natural products featuring a macrocyclic enamide skeleton.

Experimental Section

General Information. All reactions were carried out in oven- or flame-dried glassware under an argon atmosphere employing standard techniques in handling air-sensitive materials. All solvents were reagent grade. Tetrahydrofuran (THF) and toluene were freshly distilled from sodium/benzophenone under argon immediately prior to use. Dichloromethane, HMPA, and DMF were freshly distilled from calcium hydride. Methanol was distilled from magnesium turnings and iodine. Diisopropylethylamine, *N*,*N*′-dimethylethylenediamine and 2,6-lutidine were distilled over calcium hydride. Acetone was synthesis grade and used as supplied, and 99.999% purity copper(I) iodide was used. All other reagents were used as supplied. Flash chromatography was performed with silica gel 60 (particle size 35−70 μm). Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise noted. Proton NMR spectra were recorded using an internal deuterium lock at ambient temperature on a 300 MHz spectrometer. Internal references of δ_H 7.26 and δ_H 2.50 were respectively used for $CDCl_3$ and DMSO-d_6. Data are presented as follows: chemical shift (in ppm on the δ scale relative to $\delta_{TMS} = 0$), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint. = quintuplet, m = multiplet, br = broad), coupling constant (*J*/Hz), and integration. Carbon-13 NMR spectra were recorded at 75 MHz. Internal references of δ_C 77.16 and δ_C 39.52 were respectively used for $CDCl_3$ and DMSO-d_6. Optical rotations are reported as follows: $[\alpha]_D^{20}$, concentration (*c* in g/ 100 mL) and solvent.

Because of the presence of the tertiary *N*-Boc group, it was necessary to record ^{1}H and ^{13}C NMR spectra of most intermediates in DMSO-d_6 at temperatures ranging from 333 to 355K (see details below; the use of higher temperatures resulted in degradation of intermediates). Even at those temperatures, some ^{13}C peaks were poorly resolved and are denoted "broad" (br).

1-(*tert*-Butyl-dimethyl-silyloxymethyl)-4-iodo-benzene 4. To a solution of 4-iodo-benzyl alcohol (4.6 g, 19.6 mmol) in THF (50 mL) were added at 0 °C imidazole (1.75 g, 25.5 mmol) and TBSCl (3.1 g, 20.6 mmol). The resulting mixture was slowly warmed to rt over 2 h and poured into a mixture of 1 M HCl (50 mL) and ether (50 mL). The organic layer was separated, and the aqueous layer was extracted with ether. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude residue was purified by flash chromatography over silica gel (petroleum ether/AcOEt: 9/1) to yield the desired silyl ether **4** as a white solid (6.4 g, 18.4 mmol, 94%). Mp: 41 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.65 (d, J = 8.3 Hz, 2H), 7.08 (d, J = 8.3 Hz, 2H), 4.68 (s, 2H), 0.94 (s, 9H), 0.09 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 141.3, 137.6, 128.1, 92.2, 64.5, 26.0, 18.5, −5.1; IR (KBr): ν_{max} 2950, 2853, 1649, 1470, 1399, 1091, 845 cm^{-1}; EIMS: 348, 291, 261, 217.

4-Allyloxy-1-(*tert*-butyl-dimethyl-silyloxymethyl)-benzene. A pressure tube was charged with 1-(*tert*-butyl-dimethyl-silyloxymethyl)-4-iodo-benzene **4** (6.0 g, 17.2 mmol), cesium carbonate (8.4 g, 25.8 mmol), 1,10-phenanthroline (620 mg, 3.4 mmol), and copper(I) iodide (328 mg, 1.7 mmol). Toluene (17 mL) and allyl alcohol (3.5 mL, 51.7 mmol) were successively added, the pressure tube was closed, and the brownish suspension was heated to 110 °C for 12 h and cooled to rt. The crude reaction mixture was finally filtered over a plug of silica gel (washed with AcOEt) and concentrated to yield the desired aryl ether as a pale yellow liquid (4.8 g, 17.2 mmol, quant). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.14 (d, J = 8.6 Hz, 2H), 6.79 (d, J = 8.6 Hz, 2H), 5.89−6.02 (m, 1H), 5.31 (dq, J = 17.2, 1.5 Hz, 1H), 5.17 (dq, J = 10.5, 1.4 Hz, 1H), 4.58 (s, 2H), 4.42 (dt, J = 5.3, 1.4 Hz, 2H), 0.85 (s, 9H), 0.00 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.8, 133.9, 133.5, 127.6, 117.6, 114.6, 68.9, 64.8, 26.1, 18.5, −5.1; IR (neat): ν_{max} 2945, 2924, 2852, 1608, 1506, 1250, 1086, 840 cm^{-1}; EIMS: 278, 221, 147; ESIHRMS *m*/*z* calcd for $C_{16}H_{27}O_2Si$ $[M + H]^+$ 279.1780, found 279.1787.

2-Allyl-4-(*tert*-butyl-dimethyl-silyloxymethyl)-phenol 5. A 15 mL pressure tube was charged with 4-allyloxy-1-(*tert*-butyl-dimethyl-silyloxymethyl)-benzene (4.2 g, 15.1 mmol), evacuated, and backfilled with argon. The pressure tube was closed, heated to 230−240 °C for 2 h, and cooled to rt. The crude residue was purified by flash chromatography over silica gel (petroleum ether/AcOEt: 8/2) to yield the desired phenol **5** as a pale yellow oil (3.9 g, 14.0 mmol, 93%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.08 (d, J = 8.8 Hz, 1H), 7.07 (s, 1H), 6.76 (d, J = 8.8 Hz, 1H), 5.95−6.09 (m, 1H), 5.13−5.20 (m, 2H), 5.14 (s, 1H), 4.67 (s, 2H), 3.41 (d, J = 6.4 Hz, 2H), 0.95 (s, 9H), 0.11 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.2, 136.6, 133.8, 128.8, 126.1, 125.3, 116.5, 115.7, 65.0, 35.2, 26.1, 18.6, −5.0; IR (neat): ν_{max} 3324, 2929, 2848, 2755, 1496, 1255, 1091, 835 cm^{-1}; EIMS: 221, 147, 75; ESIHRMS (CI, NH_3) *m*/*z* calcd for $C_{16}H_{26}NaO_2Si$ $[M + Na]^+$ 301.1600, found 301.1621.

(*E*)-4-(*tert*-Butyl-dimethyl-silyloxymethyl)-2-propenyl-phenol 6. To a solution of **5** (2.8 g, 10.0 mmol) in toluene (25 mL) was added $RuClH(CO)(PPh_3)_3$ (440 mg, 0.46 mmol). The resulting solution was heated to 80 °C overnight and concentrated. The crude residue was purified by flash chromatography over silica gel (petroleum ether/AcOEt: 9/1) to yield the desired isomerized alkene (*E* isomer) as a pale yellow oil (2.5 g, 9.0 mmol, 90%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.15 (s, 1H), 6.94 (d, J = 8.2 Hz, 1H), 6.61 (d, J = 8.2 Hz, 1H), 6.48 (dq, J = 15.9, 1.3 Hz, 1H), 6.09 (dq, J = 15.9, 6.6 Hz, 1H), 5.11 (s, 1H), 4.55 (s, 2H), 1.80 (dd, J = 6.6, 1.3 Hz, 3H), 0.84 (s, 9H), 0.00 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.6, 133.6, 128.1, 126.3, 125.6, 125.5, 124.9, 115.7, 65.0, 26.1, 19.0, 18.6, −5.0; IR (neat): ν_{max} 3288, 2745, 1660, 1424, 1086, 835 cm^{-1}; EIMS: 278, 221, 147, 91, 75; ESIHRMS *m*/*z* calcd for $C_{16}H_{26}NaO_2Si$ $[M + Na]^+$ 301.1600, found 301.1609.

(*E*)-4-(*tert*-Butyl-dimethyl-silyloxymethyl)-1-methoxy-(2-propenyl)-benzene. To a solution of **6** (2.3 g, 8.2 mmol) in dry acetone (60 mL) were added potassium carbonate (1.5 g, 10.8 mmol) and dimethyl sulfate (0.9 mL, 9.5 mmol). The resulting greenish mixture was refluxed for 3 h, stirred overnight at rt, concentrated in vacuo, and diluted with water and CH_2Cl_2. The aqueous layer was extracted with CH_2Cl_2, and combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated. The crude residue was purified by flash chromatography over silica gel (petroleum ether/AcOEt: 95/5) to yield the desired methyl ether as a colorless

oil (2.35 g, 8.0 mmol, 98%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.37 (d, J = 2.0 Hz, 1H), 7.16 (dd, J = 8.4, 2.0 Hz, 1H), 6.83 (d, J = 8.4 Hz, 1H), 6.75 (dq, J = 15.9, 1.7 Hz, 1H), 6.25 (dq, J = 15.9, 6.6 Hz, 1H), 4.70 (s, 2H), 3.85 (s, 3H), 1.93 (dd, J = 6.6, 1.7 Hz, 3H), 0.97 (s, 9H), 0.12 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.4, 133.5, 126.9, 126.5, 125.9, 125.8, 124.7, 110.7, 64.9, 55.7, 26.1, 19.1, 18.6, −5.0; IR (neat): ν_{max} 2950, 2853, 1491, 1255, 1091, 840, 779 cm^{-1}; EIMS: 293, 279, 265, 237, 207, 193, 179, 163, 149, 135, 105, 75.

5-(*tert*-Butyl-dimethyl-silyloxymethyl)-2-methoxy-benzaldehyde 7. To a solution of (*E*)-4-(*tert*-butyl-dimethyl-silyloxymethyl)-1-methoxy-(2-propenyl)-benzene (2.2 g, 7.5 mmol) in a mixture of CCl_4 (100 mL), *t*BuOH (40 mL), and water (40 mL) was added a solution of osmium tetroxide (4 wt % solution in water, 2.4 mL, 0.4 mmol). The resulting gray solution was stirred for 15 min before adding sodium periodate (4.0 g, 18.8 mmol). The reaction mixture was vigorously stirred overnight and quenched with a 10% aqueous sodium thiosulfate solution. The aqueous layer was extracted with CH_2Cl_2, combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated. The crude residue was purified by flash chromatography over silica gel (petroleum ether/AcOEt: 95/5) to yield the desired aldehyde **6** as a gray oil (1.85 g, 6.6 mmol, 88%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.46 (s, 1H), 7.74 (d, J = 2.3 Hz, 1H), 7.56 (dd, J = 8.6, 2.3 Hz, 1H), 6.98 (d, J = 8.6 Hz, 1H), 4.68 (s, 2H), 3.92 (s, 3H), 0.93 (s, 9H), 0.09 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 190.0, 161.1, 134.1, 133.9, 126.4, 124.5, 111.8, 64.3, 55.9, 26.1, 18.5, −5.1; IR (neat): ν_{max} 2950, 2923, 2853, 1685, 1501, 1250, 1112, 840 cm^{-1}; EIMS: 281, 223, 207, 193, 149; ESIHRMS *m*/*z* calcd for $C_{15}H_{25}O_3Si$ $[M + H]^+$ 281.1573, found 281.1570.

(*Z*)-Methyl 2-*tert*-butoxycarbonylamino-3-[5-(*tert*-butyl-dimethyl-silyloxymethyl)-2-methoxy-phenyl]-acrylate 9. To a mixture of **7** (1.6 g, 5.7 mmol) and methyl 2-*tert*-butoxycarbonylamino-2-dimethoxyphosphinyl-acetate **8**[18] (2.05 g, 6.85 mmol) in dichloromethane (30 mL) at 0 °C was added *N*,*N*,*N*′,*N*′-tetramethylguanidine (3.3 mL, 8.55 mmol). The reaction mixture was then allowed to warm to room temperature, stirred overnight, and quenched with a 10% aqueous citric acid solution. The aqueous layer was extracted with CH_2Cl_2, combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated. The crude residue was purified by flash chromatography over silica gel (petroleum ether/AcOEt: 7/3) to yield the desired dehydro amino acid **9** (*Z* isomer only as demonstrated by NOE experiments) as a colorless oil (2.5 g, 5.5 mmol, 96%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.43 (d, J = 2.0 Hz, 1H), 7.30 (s, 1H), 7.28 (dd, J = 8.6, 2.1 Hz, 1H), 6.89 (d, J = 8.6 Hz, 1H), 6.41 (br s, 1H), 4.64 (s, 2H), 3.86 (s, 3H), 3.84 (s, 3H), 1.38 (s, 9H), 0.93 (s, 9H), 0.09 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.3, 156.2, 152.9, 133.6, 128.5, 127.8, 125.9, 123.7, 122.9, 111.2, 80.7, 64.6, 56.0, 52.6, 28.2, 26.1, 18.5, −5.1; IR (neat): ν_{max} 3329, 2950, 2735, 1726, 1716, 1496, 1250, 1168, 835, 779 cm^{-1}; ESIMS (positive mode): 474.2, 418.2, 374.3; ESIHRMS *m*/*z* calcd for $C_{23}H_{37}NNaO_6Si$ $[M + Na]^+$ 474.2288, found 474.2320.

(*S*)-Methyl 2-*tert*-butoxycarbonylamino-3-[5-(*tert*-butyl-dimethyl-silyloxymethyl)-2-methoxy-phenyl]-propionate 10. A mixture of **9** (1.60 g, 3.54 mmol) and (+)-1,2-bis[(2*S*,5*S*)-2,5-diethylphospholano]benzene(cyclooctadiene)-rhodium(I) trifluoromethanesulfonate ([Rh(COD){(*S*,*S*)-Et-DuPHOS}]$^+$TfO$^-$, 25 mg, 0.017 mmol) in dry and degassed methanol (20 mL) was placed under 5 atm of hydrogen and stirred for 18 h at 25 °C. The solution was concentrated under reduced pressure, and the residue was purified by flash column chromatography over silica gel (petroleum ether/AcOEt: 8/2) to yield the desired aromatic amino acid as a colorless oil (1.43 g, 3.15 mmol, 89%). Enantiomeric excess was determined by chiral HPLC analysis (Chiracel OD column, *n*-heptane/propan-2-ol: 97/3, flow rate 1.00 mL/min, λ = 254 nm), 98% ee, t_R = 6.15 min (major), 7.64 min (minor). $[\alpha]_D^{20}$ −9 (*c* 0.9, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.18 (dd, J = 8.4, 1.8 Hz, 1H), 7.02 (d, J = 1.8 Hz, 1H), 6.81 (d, J = 8.4 Hz, 1H), 5.28 (s, 1H), 5.21 (d, J = 7.4 Hz, 1H), 4.63 (s, 2H), 4.48 (app. q, J = 7.2 Hz, 1H), 3.81 (s, 3H), 3.69 (s, 3H), 3.04 (d, J = 7.0 Hz, 1H), 1.38 (s, 9H), 0.92 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.0, 156.8, 155.4, 133.6, 129.5, 126.5, 124.5, 110.3, 79.6, 64.7, 55.5, 54.2, 52.1, 32.9, 28.4, 26.1, 18.5, −5.1; IR (neat): ν_{max} 3365, 2945, 2853, 1742, 1711, 1501, 1255, 1173, 1066, 830, 768 cm^{-1}; ESIMS (positive mode): 476.3, 420.2; ESIHRMS *m*/*z* calcd for $C_{23}H_{39}NNaO_6Si$ $[M + Na]^+$ 476.2444, found 476.2458.

(*S*)-Methyl 2-(*tert*-butoxycarbonyl-methyl-amino)-3-[5-(*tert*-butyl-dimethyl-silyloxymethyl)-2-methoxy-phenyl]-propionate. To a suspension of sodium hydride (60 wt % in mineral oil, 120 mg, 2.9 mmol) in DMF (10 mL) was slowly added a solution of **10** (1.10 g, 2.42 mmol) and iodomethane (600 μL, 9.7 mmol) in DMF (18 mL). The resulting mixture was stirred for 1 h and quenched by slow addition of a saturated aqueous solution of NH_4Cl. The aqueous layer was extracted with ether, and combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated to yield the desired methylated amino acid as a colorless oil (1.11 g, 2.35 mmol, 97%). $[\alpha]_D^{20}$ −67 (*c* 1.5, $CHCl_3$); ^{1}H NMR (300 MHz, DMSO-d_6, 345 K): δ 7.14 (dd, J = 8.3, 2.1 Hz, 1H), 7.04 (d, J = 2.1 Hz, 1H), 6.92 (d, J = 8.3 Hz, 1H), 4.71−4.75 (br s, 1H), 4.63 (s, 2H), 3.80 (s, 3H), 3.68 (s, 3H), 3.20 (A of ABX syst, J = 13.9, 4.9 Hz, 1H), 2.96 (B of ABX syst, J = 13.9, 10.4 Hz, 1H), 2.64 (s, 3H), 1.28 (s, 9H), 0.91 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (75 MHz, DMSO-d_6, 345 K): δ 170.8, 156.2, 154.1, 132.5, 128.4, 125.4, 125.0, 110.1, 78.5, 63.8, 58.5, 55.1, 51.2, 31.8, 29.5, 27.4, 25.4, 17.5, −5.7; IR (neat): ν_{max} 2947, 2853, 1739, 1735, 1510, 1255, 1063, 830 cm^{-1}; ESIMS (positive mode): 490.2, 434.2; ESIHRMS *m*/*z* calcd for $C_{24}H_{41}NNaO_6Si$ $[M + Na]^+$ 490.2601, found 490.2574.

(*S*)-Methyl 2-(*tert*-butoxycarbonyl-methyl-amino)-3-(5-hydroxymethyl-2-methoxy-phenyl)-propionate. A solution of (*S*)-methyl 2-(*tert*-butoxycarbonyl-methyl-amino)-3-[5-(*tert*-butyl-dimethyl-silyloxymethyl)-2-methoxy-phenyl]-propionate (1.0 g, 2.14 mmol) in THF (26 mL) was treated with a solution of TBAF (1 M solution in THF, 3.2 mL, 3.2 mmol) at −15 °C. The resulting light yellow mixture was warmed to rt over 3 h and quenched with water. The aqueous layer was extracted with Et_2O, and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated. The crude residue was purified by flash chromatography over silica gel (petroleum ether/AcOEt: 2/8) to yield the desired alcohol as a colorless oil (756 mg, 2.14 mmol, quant). $[\alpha]_D^{20}$ −64 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, DMSO-d_6, 345 K): δ 7.16 (dd, J = 8.3, 2.1 Hz, 1H), 7.06 (d, J = 2.1 Hz, 1H), 6.90 (d, J = 8.3 Hz, 1H), 4.68−4.75 (m, 2H), 4.41 (d, J = 4.7 Hz, 2H), 3.80 (s, 3H), 3.68 (s, 3H), 3.18 (A of ABX syst, J = 13.9, 5.1 Hz, 1H), 2.98 (B of ABX syst, J = 13.9, 10.8 Hz, 1H), 2.65 (s, 3H), 1.30 (s, 9H); ^{13}C NMR (75 MHz, DMSO-d_6, 345 K): δ 170.9, 156.1, 154.1, 133.9, 128.7, 125.7, 124.9, 110.1, 78.6, 62.3, 58.6, 55.1, 51.2, 31.8, 29.5, 27.5; IR (neat): ν_{max} 3447, 2945, 1745, 1696, 1506, 1255, 1168, 1035, 815 cm^{-1}; ESIMS (positive mode): 376.3, 320.2, 276.2; ESIHRMS *m*/*z* calcd for $C_{18}H_{27}NNaO_6$ $[M + Na]^+$ 376.1736, found 376.1753.

(*S*)-Methyl 2-(*tert*-butoxycarbonyl-methyl-amino)-3-(5-formyl-2-methoxy-phenyl)-propionate 11. To a solution of (*S*)-methyl 2-(*tert*-butoxycarbonyl-methyl-amino)-3-(5-hydroxymethyl-2-methoxy-phenyl)-propionate (732 mg, 2.07 mmol) in CH_2Cl_2 (40 mL) were successively added 2,6-lutidine (260 μL, 2.23 mmol) and Dess−Martin periodinane (15 wt % solution in CH_2Cl_2, 7.6 mL, 3.7 mmol) at 0 °C. The resulting mixture was stirred for 40 min at 0 °C (a white slurry was obtained) and quenched with a mixture of 10 wt % aqueous sodium thiosulfate solution (50 mL) and saturated aqueous sodium bicarbonate solution (50 mL). The aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated. The crude residue was purified by flash chromatography over silica gel (petroleum ether/AcOEt: 1/1) to yield the desired aldehyde **9** as a colorless oil (667 mg, 1.90 mmol, 92%). $[\alpha]_D^{20}$ −56 (*c* 1.3, $CHCl_3$); ^{1}H NMR (300 MHz, DMSO-d_6, 355 K): δ 9.86 (s, 1H),

7.80 (dd, J = 8.5, 2.1 Hz, 1H), 7.67 (d, J = 2.1 Hz, 1H), 7.17 (d, J = 8.5 Hz, 1H), 4.77−4.83 (m, 1H), 3.94 (s, 3H), 3.70 (s, 3H), 3.26 (A of ABX syst, J = 14.0, 5.0 Hz, 1H), 3.09 (B of ABX syst, J = 14.0, 10.3 Hz, 1H), 2.67 (s, 3H), 1.29 (s, 9H); ^{13}C NMR (75 MHz, DMSO-d_6, 355 K): δ 190.3 and 190.2 (rotamers), 170.5, 162.1, 154.0 (br), 130.8, 130.6, 129.1, 126.4, 110.5, 78.7, 58.2 (br), 55.6, 51.3 and 51.2 (rotamers), 31.7, 29.1, 27.3; IR (neat): ν_{max} 2970, 2837, 2735, 1737, 1685, 1603, 1501, 1439, 1260, 1173, 1030 cm^{-1}; ESIMS (positive mode): 374.3, 318.2, 274.2; ESIHRMS m/z calcd for $C_{18}H_{26}NO_6$ [M + H]$^+$ 352.1760, found 352.1789.

(*S,Z*)-Methyl 2-(*tert*-butoxycarbonyl-methyl-amino)-3-[5-(2-iodo-vinyl)-2-methoxy-phenyl]-propionate. To a suspension of iodomethyltriphenyl-phosphonium iodide (1.12 g, 2.11 mmol) in THF (11 mL) was added dropwise at rt a solution of NaHMDS (2.0 M solution in THF, 1.0 mL, 2.0 mmol). The resulting red-orange solution was stirred at rt for 20 min and cooled to −78 °C before adding HMPA (1.3 mL) and a solution of **11** (550 mg, 1.56 mmol) in THF (7 mL). The reaction mixture was stirred at −78 °C for 1 h and 40 min and quenched at −78 °C by addition of a saturated aqueous solution of $NaHCO_3$. The mixture was warmed to rt, diluted with Et_2O, and filtered through a plug of Celite which was thoroughly washed with ether. The biphasic filtrate was separated, and the organic layer was dried over $MgSO_4$, filtered, and concentrated. The crude residue was purified by flash chromatography over silica gel (AcOEt/petroleum ether: 25/75) to give the desired vinyl iodide as a pale yellow oil (676 mg, 1.42 mmol, 91%). Diastereoisomeric excess was determined by analysis of crude ^{1}H NMR spectra and was found to be higher than 95%. $[\alpha]_D^{20}$ −66 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, DMSO-d_6, 355 K): δ 7.56 (dd, J = 8.5, 2.2 Hz, 1H), 7.46 (d, J = 2.2 Hz, 1H), 7.32 (d, J = 8.5 Hz, 1H), 7.01 (d, J = 8.5 Hz, 1H), 6.55 (d, J = 8.5 Hz, 1H), 4.77 (X of ABX syst, J = 10.0, 4.8 Hz, 1H), 3.85 (s, 3H), 3.69 (s, 3H), 3.24 (A of ABX syst, J = 14.0, 4.8 Hz, 1H), 3.00 (B of ABX syst, J = 14.0, 10.0 Hz, 1H), 2.68 (s, 3H), 1.29 (s, 9H); ^{13}C NMR (75 MHz, DMSO-d_6, 355 K): δ 170.6, 157.2, 154.0, 137.3 and 137.2 (rotamers), 130.2 and 130.1 (rotamers), 128.2, 127.7 and 127.6 (rotamers), 125.1, 110.1, 78.6, 77.1, 58.4 (br), 55.2, 51.2 and 51.1 (rotamers), 31.8, 29.3, 27.4; IR (neat): ν_{max} 2976, 2837, 2356, 1742, 1685, 1603, 1511, 1255, 1178, 1035, 825 cm^{-1}; ESIMS (positive mode): 498.1, 442.0, 398.1; ESIHRMS m/z calcd for $C_{19}H_{27}INO_5$ [M + H]$^+$ 476.0934, found 476.0924.

(*S,Z*)-2-(*tert*-Butoxycarbonyl-methyl-amino)-3-[5-(2-iodo-vinyl)-2-methoxy-phenyl]-propionic Acid 3. A solution of (*S,Z*)-methyl 2-(*tert*-butoxycarbonyl-methyl-amino)-3-[5-(2-iodo-vinyl)-2-methoxy-phenyl]-propionate (310 mg, 0.65 mmol) in a mixture of MeOH (2.6 mL), THF (0.7 mL), and water (0.7 mL) was treated with lithium hydroxide monohydrate (55 mg, 1.30 mmol). The resulting mixture was stirred at rt for 4 h, quenched by careful addition of 10 wt % aqueous citric acid solution, and extracted with ether. Combined organic layer were dried over $MgSO_4$, filtered, and concentrated to give the desired amino acid fragment **3** as a white sticky foam (291 mg, 0.63 mmol, 97%). $[\alpha]_D^{20}$ −38 (*c* 1.3, $CHCl_3$); ^{1}H NMR (300 MHz, DMSO-d_6, 345 K): δ 7.55 (dd, J = 8.5, 1.9 Hz, 1H), 7.45 (d, J = 1.9 Hz, 1H), 7.31 (d, J = 8.5 Hz, 1H), 6.99 (d, J = 8.5 Hz, 1H), 6.53 (d, J = 8.5 Hz, 1H), 4.73 (br s, 1H), 3.84 (s, 3H), 3.22 (A of ABX syst, J = 14.1, 4.5 Hz, 1H), 2.95 (B of ABX syst, J = 14.1, 10.8 Hz, 1H), 2.69 (s, 3H), 1.27 (s, 9H); ^{13}C NMR (75 MHz, DMSO-d_6, 345 K): δ 174.0, 157.4, 154.3 (br), 137.4, 130.2, 128.3, 127.7, 125.6, 110.1, 78.4, 77.1, 72.2, 55.2, 42.4, 31.5, 27.6; IR (neat): ν_{max} 3293, 1736, 1708, 1450, 1127, 1035, 774 cm^{-1}; ESIMS (positive mode): 484.0, 428.0, 384.1; ESIHRMS m/z calcd for $C_{18}H_{25}INO_5$ [M + H]$^+$ 462.0777, found 462.0766.

Cbz-Isoleucine-leucinamide. Benzyloxycarbonyl-protected isoleucine (Z-Ile-OH, 2.0 g, 7.5 mmol), leucinamide hydrochloride (H-Leu-NH_2,HCl, 1.26 g, 7.5 mmol), and 1-hydroxy-7-azabenzotriazole (HOAt, 1.02 g, 7.5 mmol) were dissolved in DMF (50 mL). The reaction mixture was cooled to 0 °C, 1-(3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride (EDC, 1.44 g, 7.5 mmol) and *N*-methylmorpholine (2.1 mL, 18.7 mmol) were successively added at 0 °C, and the solution was stirred for 16 h while progressively warmed to rt. The yellow slurry was finally concentrated and diluted with 1 M HCl aqueous solution. The aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated to give the desired dipeptide (2.3 g, 6.1 mmol, 81%) as a white solid. Mp: 212 °C; $[\alpha]_D^{20}$ −20 (*c* 0.3, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.87 (d, J = 8.3 Hz, 1H), 7.31−7.43 (m, 7H), 7.01 (s, 1H), 5.07 (s, 2H), 4.26−4.33 (m, 1H), 3.92 (t, J = 8.0 Hz, 1H), 1.70−1.77 (m, 1H), 1.54−1.67 (m, 1H), 1.41−1.51 (m, 3H), 1.07−1.23 (m, 1H), 0.91 (d, J = 6.5 Hz, 3H), 0.81−0.87 (m, 9H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 173.9, 170.9, 156.1, 137.1, 128.3, 127.8, 127.6, 65.4, 59.3, 50.7, 41.0, 36.3, 24.4, 24.2, 23.0, 21.6, 15.4, 10.9; IR (KBr): ν_{max} 3385, 3314, 2945, 1670, 1639, 1537, 1235, 702 cm^{-1}; ESIHRMS m/z calcd for $C_{20}H_{32}N_3O_4$ [M + H]$^+$ 378.2393, found 378.2401.

Isoleucine-leucinamide 12. A slurry of Cbz-isoleucine-leucinamide (600 mg, 1.59 mmol) in 95% ethanol (25 mL) was treated with palladium on carbon (10 wt % on activated carbon, 100 mg) and stirred under an atmosphere of hydrogen for 1 h. The mixture was filtered over a plug of Celite and concentrated. The crude residue was purified by flash chromatography over silica gel (AcOEt/EtOH/30% aq NH_3: 90/9/1) to give the desired peptide as a white solid (364 mg, 1.50 mmol, 94%). Mp: 121 °C; $[\alpha]_D^{20}$ −25 (*c* 2.0, MeOH); ^{1}H NMR (300 MHz, MeOH-d_4): δ 4.43 (dd, J = 9.1, 5.8 Hz, 1H), 3.21 (d, J = 5.4 Hz, 1H), 1.44−1.77 (m, 5H), 1.09−1.26 (m, 1H), 0.88−0.98 (m, 12H); ^{13}C NMR (75 MHz, MeOH-d_4): δ 177.4, 177.0, 60.9, 52.5, 42.3, 40.2, 25.9, 25.3, 23.4, 21.9, 16.1, 11.9; IR (KBr): ν_{max} 3411, 3350, 2966, 1706, 1680, 1634, 1506, 1414, 850, 595 cm^{-1}; ESIMS (positive mode): 266.3; ESIHRMS m/z calcd for $C_{12}H_{26}N_3O_2$ [M + H]$^+$ 244.2025, found 244.2035.

(*Z*)-[*N*-Boc-*N*-Methyl-5-(2-iodo-vinyl)-2-methoxy-phenylalanyl]-isoleucine-leucinamide 13. To a solution of **3** (199 mg, 0.43 mmol) in DMF (1 mL) were successively added at 0 °C diisopropylethylamine (83 μL, 0.47 mmol) and (benzotriazol-1-yloxy)-tris-(dimethylamino)phosphonium hexafluorophosphate (BOP, 200 mg, 0.45 mmol). After stirring for 30 min at 0 °C, **12** (127 mg, 0.52 mmol) was added. The resulting mixture was slowly warmed to rt, stirred overnight and quenched with a 10% aqueous citric acid solution. The aqueous layer was extracted with ether, combined organic layers were successively washed with a saturated aqueous solution of $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and concentrated. The crude residue was purified by flash chromatography over silica gel (AcOEt/30% aq NH_3: 99/1) to yield the desired tripeptide **13** as a white solid (272 mg, 0.40 mmol, 92%). Mp: 89 °C; $[\alpha]_D^{20}$ −36 (*c* 0.7, $CHCl_3$); ^{1}H NMR (300 MHz, DMSO-d_6, 345 K): δ 7.70 (d, J = 8.0 Hz, 1H), 7.57 (dd, J = 8.5, 2.2 Hz, 1H), 7.44 (d, J = 2.2 Hz, 1H), 7.31 (d, J = 8.5 Hz, 1H), 7.14 (d, J = 8.7 Hz, 1H), 6.81 (br s, 2H), 6.55 (d, J = 8.5 Hz, 1H), 4.87 (X of ABX syst, J = 10.2, 4.8 Hz, 1H), 4.21−4.32 (m, 2H), 3.84 (s, 3H), 3.12 (A of ABX syst, J = 14.5, 4.7 Hz, 1H), 2.95 (B of ABX syst, J = 14.5, 10.2 Hz, 1H), 2.71 (s, 3H), 1.76−1.87 (m, 1H), 1.55−1.70 (m, 1H), 1.39−1.53 (m, 3H), 1.30 (s, 9H), 1.03−1.11 (m, 1H), 0.91 (d, J = 6.5 Hz, 3H), 0.81−0.88 (m, 9H); ^{13}C NMR (75 MHz, DMSO-d_6, 345 K): δ 173.2, 170.0, 169.5, 157.2, 154.5 (br), 137.4, 129.9, 128.2, 127.3, 125.5, 110.0, 78.7, 77.3, 57.9 (br), 56.7, 55.2, 50.8 and 50.7 (rotamers), 40.7, 36.3, 30.2 (br), 28.1, 27.5, 23.9, 22.4, 21.3, 15.0, 10.3; IR (KBr): ν_{max} 3288, 2955, 1675, 1644, 1506, 1260, 1153, 1020, 820 cm^{-1}; ESIMS (positive mode): 709.3, 581.4; ESIHRMS m/z calcd for $C_{30}H_{48}IN_4O_6$ [M + H]$^+$ 687.2619, found 687.2577.

***N*-Boc-Abyssenine A 14.** A 50 mL flask was charged with iodoamide **13** (200 mg, 0.29 mmol), copper(I) iodide (11.1 mg, 0.06 mmol), and cesium carbonate (142 mg, 0.43 mmol). The flask was evacuated under high vacuum, backfilled with argon, and closed with a rubber septa. Dry and degassed THF (36 mL) and *N,N*′-dimethylethylene-1,2-diamine (13 μL, 0.12 mmol) were next added,

the rubber septa was replaced by a glass stopper, and the light blue suspension was sonicated for 2 min before being heated to 63 °C for 3 days. The reaction mixture was cooled to rt and filtered over a plug of silica gel (washed with AcOEt) and concentrated. The crude residue was purified by flash chromatography over silica gel (AcOEt/petroleum ether: 35/65) to give the desired cyclized product **14** (134 mg, 0.24 mmol, 83%) as a white solid. Mp: 100 °C; $[\alpha]_D^{20}$ −144 (*c* 0.3, $CHCl_3$); ^{1}H NMR (300 MHz, DMSO-d_6, 345 K): δ 8.41 (d, J = 10.7 Hz, 1H), 8.05 (d, J = 8.4 Hz, 1H), 7.26 (d, J = 7.7 Hz, 1H), 7.01−7.05 (m, 3H), 6.72 (app. t, J = 9.8 Hz, 1H), 5.69 (d, J = 9.8 Hz, 1H), 4.74 (d, J = 8.4 Hz, 1H), 4.34 (app. q, J = 7.5 Hz, 1H), 4.02 (t, J = 7.5 Hz, 1H), 3.82 (s, 3H), 3.26 (dd, J = 13.8, 10.9 Hz, 1H), 2.83 (dd, J = 13.8, 1.3 Hz, 1H), 2.81 (s, 3H), 1.68−1.83 (m, 1H), 1.41−1.61 (m, 3H), 1.47 (s, 9H), 1.03−1.21 (m, 1H), 0.90 (d, J = 6.1 Hz, 3H), 0.86 (d, J = 6.7 Hz, 6H), 0.83 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6, 345 K): δ 170.9, 170.0, 169.7, 155.5, 154.8 (br), 127.8, 127.5, 127.1, 126.9, 120.3, 111.4, 109.8, 79.3, 58.7, 57.6 (br), 55.4, 51.8, 40.3, 35.2, 29.8 (br), 27.7, 26.3 (br), 24.3, 23.9, 22.3, 20.6, 15.0, 9.9; IR (KBr): ν_{max} 3409, 2963, 1692, 1640, 1459 cm^{-1}; ESIMS (positive mode): 581.3, 481.3; ESIHRMS *m*/*z* calcd for $C_{30}H_{46}N_4NaO_6$ $[M + Na]^+$ 581.3315, found 581.3283.

Abyssenine A 1. To a solution of **14** (50 mg, 0.089 mmol) in dichloromethane (4.0 mL) were added at −20 °C 2,6-lutidine (10.5 μL, 0.089 mmol) and a solution of trimethylsilyl trifluoromethanesulfonate (1.4 M solution in dichloromethane, 255 μL, 0.356 mmol). The resulting light pink solution was stirred for 2 h while progressively warmed to 0 °C. The mixture was next hydrolyzed at 0 °C by addition of a saturated aqueous solution of $NaHCO_3$ and diluted with dichloromethane. The aqueous layer was extracted with dichloromethane, and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated. The crude residue was purified by flash chromatography over silica gel (CH_2Cl_2/MeOH/30% aq NH_3: 94/5/1) to give the desired synthetic abyssenine A **1** (39 mg, 0.085 mmol, 95%) as a white solid. R_f: 0.32 (Merck-Kiesegel 60F_{254} TLC plates, CH_2Cl_2/ MeOH/ 30% aq NH_3: 94/5/1); Mp: 241 °C {lit.: Mp: 237−239 °C};[13a] $[\alpha]_D^{20}$ +163 (*c* 0.40, $CHCl_3$) {lit.: natural abyssenine A: $[\alpha]_D^{20}$: +160 (*c* 0.22, $CHCl_3$)};[13a] $[\alpha]_D^{20}$ −60 (*c* 0.15, MeOH) {lit.: natural abyssenine A: $[\alpha]_D^{20}$: −58 (*c* 0.1, MeOH)};[13a] ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.43 (d, J = 7.5 Hz, 1H), 8.47 (d, J = 11.3 Hz, 1H), 8.16 (d, J = 7.2 Hz, 1H), 7.14 (d, J = 2.1 Hz, 1H), 7.01 (dd, J = 8.5, 2.2 Hz, 1H), 6.88 (d, J = 8.6 Hz, 1H), 6.83 (dd, J = 11.3, 9.6 Hz, 1H), 5.60 (d, J = 9.6 Hz, 1H), 4.47 (ddd, J = 11.1, 7.7, 3.6 Hz, 1H), 3.86 (s, 3H), 3.46 (dd, J = 13.6, 6.1 Hz, 1H), 3.25−3.32 (m, 2H), 3.04 (dd, J = 13.6, 2.3 Hz, 1H), 2.47−2.60 (m, 1H), 2.48 (s, 3H), 2.18 (br s, 1H), 1.92−2.00 (m, 1H), 1.71−1.84 (m, 2H), 1.52 (dqd, J = 10.6, 7.5, 3.2 Hz, 1H), 1.14 (dqd, J = 10.6, 7.5, 7.5 Hz, 1H), 1.02 (d, J = 6.3 Hz, 3H), 0.96 (d, J = 6.3 Hz, 3H), 0.90 (d, J = 6.8 Hz, 3H), 0.86 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.2, 172.3, 170.1, 156.3, 129.9, 129.04, 128.99, 125.2, 120.5, 111.7, 109.8, 66.3, 65.8, 55.8, 52.5, 41.2, 36.6, 33.4, 31.3, 25.9, 25.2, 23.5, 21.1, 15.4, 9.7; UV λ_{max} (log ϵ): 278 (4.25); IR (KBr): ν_{max} 3407, 3278, 2960, 2858, 1685, 1640, 1465, 1255, 1122, 1030 cm^{-1}; EIMS: 458, 431, 415, 400, 386, 356, 345, 302, 296, 259, 231, 205, 183, 163, 155, 86; ESIHRMS *m*/*z* calcd for $C_{25}H_{39}N_4O_4$ $[M + H]^+$ 459.2971, found: 459.2953.

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Supporting Information Available: Copies of ^{1}H and ^{13}C NMR spectra for all intermediates and abyssenine A. ^{1}H−^{1}H COSY and ^{1}H−^{13}C HSQC NMR spectra of synthetic abyssenine A. Abyssenine A spectral data compared to reported data. This material is available free of charge via the Internet at http://pubs.acs.org.

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