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One-Pot Hydrogenation Conditions for a Sequential Process to (+)-Monomorine

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Abstract: (+)-Monomorine has been synthesized under mild hydrogenation conditions initiating deprotection followed by intramolecular, sequential reductive amination reactions. The precursors could be prepared concisely using *B*-alkyl Suzuki cross coupling of a chiral homoallylamine and a vinyl iodide or an iodofuran derivative.

The indolizidine alkaloid monomorine, a trail pheromone of the Pharaoh's ant, is a fused bicyclic tertiary amine molecule isolated from *Monomorium pharaonis* L. by Ritter.[1] Many synthetic methods have been developed for the skeleton with the correct arrangement of chiral centers adjacent to the nitrogen atom.[2] As we have been interested in an intramolecular reductive amination approach for the indolizidine skeleton,[3] we wanted to arrange an asymmetric sequential reductive pathway to (+)-monomorine.

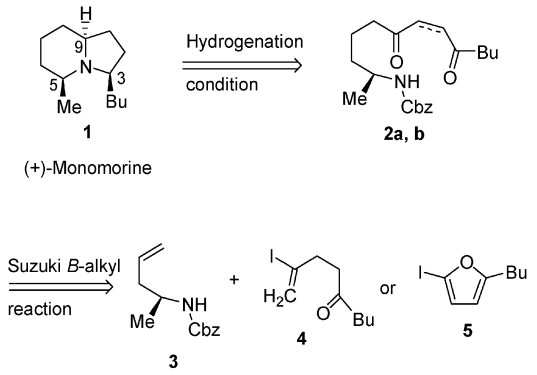
The previous results for the molecule have shown that in the course of reductive reaction the stereocenter at C5 afforded high selectivity of the two developing C3 and C9 centers, whereas the center at C3 gave poor selectivity.[2] In Shawe's racemic synthesis of monomorine, they used the 1,5-dicarbonyl precursor in which the stereocenter arranged at C3 should control the other ones in the reductive amination, and actually the reaction yielded 1:1 diastereomeric mixture.[2b] Therefore, we considered that intermediate **2a** or **2b** would be a proper precursor in which *N*-Cbz and 1,4-dicarbonyl groups are arranged, and hydrogenation conditions should trigger the desired transformation selectively and consecutively.[3] The precursors were considered to be prepared readily by *B*-alkyl Suzuki coupling[4] of homoallylamine **3** and the iodide compound **4** or **5** (Scheme 1).

The homoallylamine **3** was prepared from the chiral *β*-amino methyl butanoate **6**, which was made by the known procedure using (*S*)-lithium *N*-benzyl-α-methybenzylamide.[5] Protection of the amino ester **6** with CbzCl (77% yield) was followed by DIBAL-H reduction to afford aldehyde **7** in 45% yield, and the Wittig reaction of **7** provided **3** in 67% yield (Scheme 2).

The coupling partner, internal alkenyl iodide **4**, was made selectively via a four-step sequence; protection of 1-nonyn-5-ol with Ac_2O (97% yield), treatment with HI, generated in situ,[6] affording internal iodoalkenyl acetate **9** as a major isomer in a 10:1 mixture of inseparable regioisomers (69% yield), and deprotection (81% yield) followed by PDC oxidation (83% yield) (Scheme 3).

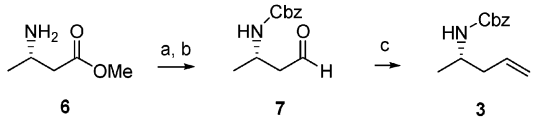
The Suzuki cross coupling of **3** and **4** provided the methylene compound **10** in 76% yield, and conversion of **10** to the carbonyl precursor **2a** was achieved by oxidative cleavage using OsO_4 and Oxone in DMF in 58% yield (Scheme 4).[7] For the desired transformation of **2a**, 1 atm of H_2 for 1 h at room temperature was indeed enough to afford 50% of (+)-monomerine (**1**) as a main product after

SCHEME 1



1 (+)-Monomorine; **2a, b**; **3**; **4**; **5**

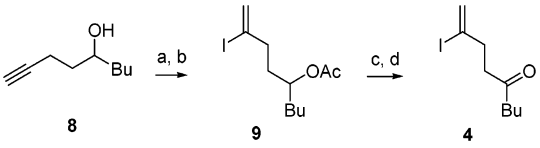
SCHEME 2[a]



6; **7**; **3**

[a] Key: (a) CbzCl, $NaHCO_3$, $MeOH/H_2O$, rt, 77%; (b) DIBAL-H, toluene, −78 °C, 45%; (c) $Ph_3P{=}CH_2$, THF/DMF, HMPA, 0 °C, 67%.

SCHEME 3[a]



8; **9**; **4**

[a] Key: (a) Ac_2O, Et_3N, DMAP, CH_2Cl_2, 97%; (b) TMSCl, NaI, H_2O, CH_3CN, rt, 69%; (c) NaOMe, MeOH, rt, 81%; (d) PDC, CH_2Cl_2, rt, 83%.

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(3) Kim, G.; Jung, S.-d.; Kim, W.-j. *Org. Lett.* **2001**, *3*, 2985.

(4) (a) Miyamura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. (b) Suzuki, A. *J. Organomet. Chem.* **1999**, *576*, 147. (c) Chemler, S. R.; Trauner, D.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 4544.

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(6) Kamiya, N.; Chikami, Y.; Ishii, Y. *Synlett* **1990**, 675.

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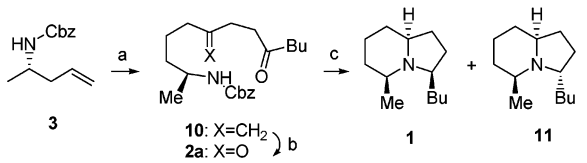
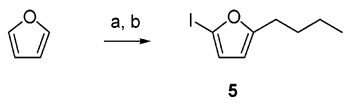
SCHEME 4[a]



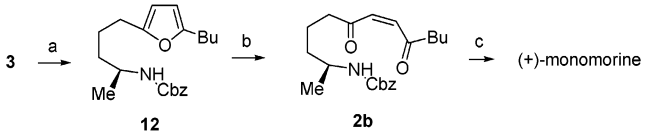
[a] Key: (a) (i) 9-BBN-H, THF, rt, (ii) **4**, $Pd(dppf)Cl_2$, $AsPh_3$, Cs_2CO_3, DMF, rt, 76%; (b) OsO_4, Oxone, DMF, rt, 58%; (c) 10% Pd/C, H_2, MeOH, rt, 50%.

SCHEME 5[a]



[a] Key: (a) (i) *n*-BuLi, THF, −78 to −20 °C, (ii) BuI, −20 °C, 75%; (b) (i) n-BuLi, THF, −78 to 0 °C, (ii) I_2, 78%, −78 °C.

SCHEME 6[a]



[a] Key: (a) (i) 9-BBN-H, THF, rt, (ii) **5**, $Pd(PPh_3)_4$, $AsPh_3$, Cs_2CO_3, DMF, rt, 95%; (b) MMPP, $EtOH/H_2O$,rt, 61%; (c) 10% Pd/C, H_2, MeOH, rt, 45%.

purification along with less than 4% of the known epimeric compound **11**, indolizidine 195B.[8]

As the 1,4-dicarbonyl group proved suitable for the transformation, we planned an alternative direct way to a related precursor. We envisioned that a suitable furan derivative would be readily prepared by the Suzuki coupling and this furan would be transformed to a α,β-unsaturated 1,4-dicarbonyl compound.[9] For the purpose, 2-iodo-5-butylfuran (**5**) was readily prepared in quantity by the conventional substitution reaction condition of furan derivatives,[10] deprotonation with *n*-BuLi followed by addition of BuI (75%), and the same deprotonation condition for the resulting 2-butylfurane followed by I_2 addition (78%) (Scheme 5).

The Suzuki coupling of **3** and **5** gave out **12** in 95% yield when using $Pd(PPh_3)_4$ as a catalyst. Conversion of the furan derivative **12** to **2b** was then performed by treatment with magnesium monoperoxyphthalate at room temperature in 61% yield (Scheme 6).[9b] As expected, the same hydrogenation condition transformed the precursor **2b** to (+)-monomorine in 5 h, affording 45% yield after purification. The two synthetic (+)-monomorine have shown satisfactory spectral data (^1H and ^{13}C NMR and MS).[2a]

In summary, we have described the concise synthesis of (+)-monomerine from the precursors **2a** and **2b**, which have been prepared using Suzuki coupling reaction. The mild hydrogenation condition transformed the intermediates to (+)-monomorine through deprotection followed by consecutive reductive amination reactions. However, it is not still clear whether **2a** and **2b** converged to a common intermediate prior to providing the product. Further application of this strategy for related compounds is under study.

Experimental Section

All reactions were performed in oven-dried glassware with magnetic stirring. Commercial grade reagents were used without further purification except for chlorotrimethylsilane (TMSCl), which was distilled from calcium hydride. Anhydrous THF was distilled from Na/benzophenone. The melting points are uncorrected. TLC analysis was performed using glass plate precoated with silica gel $60F_{254}$. Flash column chromatography was performed with 230−400 mesh silica gel. ^1H NMR spectra were obtained on 300 and 500 MHz spectrometers. NMR spectra were recorded in parts per million (δ) relative to the peak for tetramethylsilane ($\delta = 0.00$) as an internal standard. Optical rotations were obtained on a digital polarimeter.

(3*S*)-3-(*N*-Benyloxycarbonylamino)butyl Aldehyde (7). To a solution of amino ester **6** (0.260 g, 2.20 mmol) in 10 mL of 50% aqueous MeOH were added $NaHCO_3$ (0.460 g, 5.50 mmol) and CbzCl (0.560 g, 3.30 mmol) at 0 °C, the mixture was stirred for 5 h at rt, extra CbzCl (0.560 g, 3.30 mmol) was added, and the mixture was stirred for an additional 4 h. To the resulting mixture were added saturated NH_4Cl solution and $NaHCO_3$ solution, and the solution was extracted with EtOAc (5 mL × 3). The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude product was purified by column chromatography of silica gel (50 g, elution with hexane/EtOAc = 2:1) to provide 0.420 g (77%) of *N*-Cbz ester intermediate: ^1H NMR (300 MHz, $CDCl_3$) δ 7.25−7.33 (m, 5H), 5.23 (bs, 1H), 5.07 (s, 2H), 4.13 (dt, $J = 5.1, 6.6$ Hz, 1H), 4.11 (s, 3H), 2.48 (d, $J = 5.1$ Hz, 1H), 1.24 (d, $J = 6.6$ Hz, 3H).

The ester (0.420 g, 1.70 mmol) was dissolved in anhydrous toluene (17 mL), and DIBAL-H (1.36 mL, 1.5 M in toluene, 2.04 mmol) was added slowly at −78 °C under N_2. The mixture was stirred for 30 min at −78 °C, and MeOH was added to the solution to destroy excess DIBAL-H. After the reaction mixture was diluted with EtOAc, the organic layer was washed with water, dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by column chromatography of silica gel (50 g, elution with hexane/EtOAc = 2:1) to provide 0.170 g (45%) of *N*-Cbz-amino aldehyde **7**: ^1H NMR (300 MHz, $CDCl_3$) δ 9.74 (s, 1H), 7.28−7.35 (m, 5H), 5.10 (s, 2H), 5.06 (bs, 1H), 4.18 (m, 1H), 2.02 (dd, $J = 6.6, 6.6$ Hz, 2H), 1.14 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.8, 171.1, 136.3, 128.4(2), 128.1(2), 66.6, 60.3, 42.8, 20.9; IR (neat) 3334, 1719, 1690, 1533 cm^{-1}; mass spectrum (EI) *m/z* 221 (M^+).

(2*S*)-2-(*N*-Benyloxycarbonylamino)-4-butene (3). A 20 mL, one-necked, round-bottomed flask equipped with a rubber septum pierced with an argon inlet needle was charged with a solution of methyltriphenylphosphonium iodide (0.220 g, 0.544 mmol) in 4 mL of THF. To this resulting solution was added *n*-BuLi (2.5 M in hexane, 0.24 mL, 0.58 mmol) slowly at 0 °C. After 10 min of stirring at 0 °C, 0.190 mL of HMPA was added, and the solution was stirred for 50 min. To this mixture was added a solution of aldehyde **7** (0.080 g, 0.362 mmol) in 6 mL of DMF. After the resulting solution was stirred at rt overnight, it was diluted with 5 mL of EtOAc and washed with water twice (10 mL × 2). The organic layer was dried over $MgSO_4$, filtered, and concentrated. Purification by column chromatography of silica gel (elution with hexane/EtOAc = 2:1) provided 0.054 g of homoallylic amine **3** (67%): $[\alpha]^{24}_D = -13.0$ (*c* 1.02, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.26−7.37 (m, 5H), 5.75 (m, 1H), 5.10 (s, 2H), 5.03−5.08 (m, 2H), 4.60 (bs, 1H), 3.79 (m, 1H), 2.63 (d, $J = 5.1$ Hz, 2H), 1.24 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.7, 136.7, 134.3, 128.4 (3), 128.0 (2), 117.8, 66.4, 46.5, 41.1, 20.4; IR (neat) 3327, 2972, 1697, 1586 cm^{-1}; mass spectrum (EI) *m/z* 219 ($M^+ - 1$); exact mass calcd for $C_{13}H_{16}NO_2$ ($M^+ - 1$) 218.1180, found 218.1167.

2-Iodo-5-acetoxy-1-nonene (9). To a solution of 1-nonyn-5-ol **8** (0.960 g, 6.85 mmol) and Et_3N (2.87 mL, 20.6 mmol) in

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20 mL of methylene chloride were added acetic anhydride (0.766 mL, 8.22 mmol) and a catalytic amount of DMAP (5%). The solution was stirred at rt overnight and diluted with 10 mL of methylene chloride. The organic layer was washed with water, 2% of aqueous HCl solution, water again, and brine. Drying over $MgSO_4$ was followed by filtration and concentration, and purification by silica gel column chromatography provided 1.21 g (97%) of an acetate as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.88 (m, 1H), 2.15 (m, 2H), 1.97 (s, 3H), 1.88 (t, J = Hz, 1H), 1.70 (m, 2H), 1.48 (m, 2H), 1.23 (m, 4H), 0.82 (t, J = 6.94 Hz, 3H).

To an acetonitrile solution (40 mL) containing NaI (2.86 g, 19.1 mmol) and TMSCl (2.42 mL, 19.1 mmol) was added water (0.17 mL, 9.55 mmol), and the mixture was stirred at rt for 10 min. To this resulting mixture was added the acetate intermediate in 2 mL of acetonitrile via syringe, and the solution was stirred at rt for 1 h. After the addition of water to the mixture and dilution with diethyl ether, the organic layer was washed with saturated sodium thiosulfate solution and dried over $MgSO_4$. Filtration and concentration were followed by separation by column chromatography on silica gel (40 g, elution with hexane/EtOAc = 100:1) to afford 3.36 g of the iodoacetate **9** (69%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.00 (d, J = 1.20 Hz, 1H), 5.67 (m, J = 1.20 Hz, 1H), 4.86 (m, 1H), 2.39 (m, 2H), 2.02 (s, 3H), 1.75 (m, 2H), 1.52 (m, 2H), 1.27 (m, 4H), 0.87 (t, J = 6.96 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 125.8, 111.0, 72.9, 41.3, 33.5, 27.4, 22.5, 21.2, 13.9; IR (neat) 1735, 1234 cm^{-1}; mass spectrum (EI) m/z 251 (M^+ − OAc); exact mass calcd for $C_{11}H_{19}IO_2$ 310.0430, found 218.0420.

2-Iodo-5-oxo-1-nonene (4). The mixture of iodoacetate **9** (3 g, 9.67 mmol) in 6 mL of MeOH and 3.14 g of NaOMe (3.14 g, 58 mmol) was stirred at rt overnight under N_2 atmosphere. After dilution of the mixture with diethyl ether, the organic layer was washed with saturated NH_4Cl solution twice, water, and brine and dried over $MgSO_4$. Filtration was followed by concentration and silica gel column chromatography (elution with hexane/EtOAc = 30:1) to afford 2.1 g of an alcohol intermediate (81%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.04 (d, J = 1.20 Hz, 1H), 5.68 (d, J = 1.20 Hz, 1H), 3.60 (m, 1H), 2.50 (m, 2H), 1.30−1.68 (m, 8H), 0.88 (t, J = 6.96 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 125.6, 112.1, 70.4, 41.6, 37.4, 36.8, 27.7, 22.7, 14.0; IR (neat) 3320, 2927 cm^{-1}; mass spectrum (EI) m/z 268 (M^+); exact mass calcd for $C_9H_{17}IO$ 268.0324, found 267.0322.

To a solution of pyridinium dichromate (2.95 g, 7.83 mmol) in CH_2Cl_2 containing 4 Å molecular sieves (1 g) was added the alcohol obtained (0.700 g, 2.61 mmol) in 1 mL of methylene chloride. The mixture was stirred at rt overnight, filtered through Celite on a glass filter, concentrated, and separated by silica gel column chromatography (elution with hexane/EtOAc = 50:1) to afford 2.43 g of the iodoketone (83%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.09 (d, J = 1.1 Hz, 1H), 5.68 (d, J = 1.1 Hz, 1H), 2.65 (t, J = 6.90 Hz, 2H), 2.45 (t, J = 7.40 Hz, 2H), 1.59 (t, J = 7.40 Hz, 2H), 1.33 (m, 2H), 1.27 (m, 4H), 0.94 (t, J = 7.35 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.0, 126.4, 110.2, 42.5, 42.1, 41.1, 25.9, 22.3, 13.8; IR (neat) 2955, 1712 cm^{-1}; mass spectrum (EI) m/z 267 (M^+ + H); exact mass calcd for $C_9H_{15}IO$ ((M^+ + H) 267.0246, found 267.0254.

(2*S*)-2-(*N*-Benyloxycarbonylamino)-6-methylene-9-oxotridecane (10). To a solution of homoallylamine **3** (0.283 g, 1.30 mmol) in 5 mL of THF was added 9-BBN (0.317 g, 1.30 mmol), the solution was stirred at rt for 2 h under Ar, and water (234 μL, 130 mmol) was added. After 30 min, the resulting solution was cannulated to a solution of **4** (0.378 g, 1.42 mmol), Ph_3As (40 mg, 0.130), Cs_2CO_3 (0.847 g, 2.60 mmol), water (234 μL, 130 mmol) in 10 mL of DMF in a 50 mL, one-necked, round-bottomed flask. The combined mixture was stirred at rt for 6 h and diluted with 50 mL of EtOAc. The organic layer was washed with saturated NH_4Cl solution (20 mL), saturated $NaHCO_3$ solution (20 mL), water (10 mL), and brine and dried over $MgSO_4$. After filtration and concentration, the crude product was separated by column chromatography using 50 g of silica gel and eluting solvents, hexane/EtOAc = 10:1, to afford 0.353 g of **10** (76%): $[\alpha]^{24}_D$ = 1.06 (*c* 1.09, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26−7.36 (m, 5H), 5.08 (s, 2H), 4.72 (s, 1H), 4.67 (s, 1H), 4.63 (bs, 1H), 2.53 (t, J = 7.5 Hz, 2H), 2.41 (t, J = 7.0 Hz, 2H), 2.25 (t, J = 7.0 Hz, 2H), 2.01 (m, 2H), 1.55 (t, J = 7.5 Hz, 2H), 1.40−1.50 (m, 4H), 1.30 (dt, J = 7.5, 7.5 Hz, 2H), 1.14 (d, J = 6.0 Hz, 3H), 0.90 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.7, 155.7, 148.0, 136.6, 128.5 (3), 128.0 (2), 109.2, 66.4, 47.0, 42.6, 40.8, 32.0, 29.5, 26.2, 23.9, 22.3, 21.6, 21.2, 13.8; IR (neat) 2924, 1708, 1241 cm^{-1}; mass spectrum (EI) m/z 359 (M^+); exact mass calcd for $C_{22}H_{33}NO_3$ 359.2460, found 359.2480.

(2*S*)-2-(*N*-Benyloxycarbonylamino)-6, 9-dioxotridecane (2a). To a solution of methyleneamine **10** (0.500 g, 1.40 mmol) in 7 mL of DMF was added OsO_4 (0.174 mL, 0.014 mmol, 2.5% in *t*-BuOH) at rt. After the mixture was stirred for 5 min at rt, oxone (3.42 g, 5.56 mmol) was added slowly and the resulting solution was stirred for 3 h at rt. To this solution was added Na_2SO_3 (1.05 g, 8.34 mmol), and the solution was stirred until the color turned dark. The mixture was diluted with 30 mL of EtOAc, and the organic layer was washed with 1 N HCl three times and brine and dried over Na_2SO_4. Filtration was followed by concentration, and the crude product was purified by silica gel column chromatography (elution with hexane/EtOAc = 5:1) to afford 0.30 g of **2a** (58% yield): $[\alpha]^{24}_D$ = −2.02 (*c* 1.00, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27−7.35 (m, 5H), 5.10 (s, 2H), 4.72 (bs, 1H), 2.66 (t, J = 7.5 Hz, 2 × 2H), 2.46 (t, J = 7.5 Hz, 2H), 2.44 (t, J = 7.5 Hz, 2H), 1.53−1.58 (m, 4H), 1.41 (m, 2H), 1.30 (m, 2H), 1.13 (d, J = 6.5 Hz, 3H), 0.90 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.7, 209.3, 155.7, 136.6, 128.4 (3), 128.0 (2), 66.4, 46.8, 42.4, 42.2, 36.2, 35.9, 35.9, 25.8, 22.2, 21.1, 20.0,13.8; IR (neat) 1698, 1686, 1545 cm^{-1}; mass spectrum (EI) m/z 361 (M^+); exact mass calcd for $C_{21}H_{31}NO_4$ 361.2253, found 361.2252.

2-Iodo-5-butylfuran (5). To a solution of furan (16 mL, 0.216 mol) in 300 mL of THF in a 1 L round-bottomed flask was added 56 mL of *n*-BuLi (0.14 mol, 2.5 M in hexane) slowly at −78 °C under Ar gas. The solution was warmed to −20 °C and stirred for 1 h at the temperature. After iodobutane (20 g, 0.108 mol) was added slowly to the mixture at −20 °C, the solution was warmed to rt and stirred for 2 h. Slow addition of water (100 mL) was followed by extraction with diethyl ether (250 mL × 2). Drying over $MgSO_4$, filtration, and concentration afforded the crude product, which was purified by short silica gel filtration (elution with hexane) and simple distillation (40 °C/20 mmHg) to obtain 10 g of 2-butylfuran (75%) as a colorless oil.

The compound (8.5 g, 68.5 mmol) was dissolved in 250 mL of THF and cooled to −78 °C. To this solution was added slowly 35 mL of *n*-BuLi (89.1 mmol, 2.5 M in hexane), and the resulting solution was warmed to 0 °C, stirred for 10 min at 0 °C, and cooled again to −78 °C. To this solution was added slowly iodine (22.6 g, 89 mmol) in 50 mL of THF, and the solution was warmed slowly to 0 °C and stirred for 2 h at 0 °C. After addition of 100 mL of water, the solution was extracted with ether (250 mL × 2). The organic layer was washed with aqueous $Na_2S_2O_3$ solution (60 mL) and water, dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by silica gel column chromatography (elution with hexane) to afford 13.3 g of **5** (78%) as a pale brownish oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.39 (d, J = 3.2 Hz, 1H), 5.90 (m, 1H), 2.63 (t, J = 7.74 Hz, 2H), 1.59 (tt, J = 7.20, 7.20 Hz, 2H), 1.33 (tq, J = 7.20, 7.32 Hz, 2H), 0.89 (t, J = 7.32 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.2, 120.6, 108.0, 84.2, 30.1, 27.9, 22.1, 13.7; IR (neat) 1382, 1066 cm^{-1}; mass spectrum (EI) m/z 250 (M^+).

2-((2*S*)-2-*N*-Benzyloxycarbonylaminopentyl)-5-butylfuran (12). To a solution of **3** (0.50 g, 2.5 mmol) in 8 mL of THF was added 9-BBN (0.61 g, 2.5 mmol), and then the solution was stirred at rt for 2 h under argon gas. To the solution was added water (0.50 g, 28 mmol), and the solution was stirred for 20 min. The resulting solution was cannulated to a solution of **5** (0.750 g, 3.0 mmol), $Pd(PPh_3)_4$ (0.24 g, 0.21 mmol), Cs_2CO_3 (1.30 g, 4.0 mmol), Ph_3As (0.064 g, 0.21 mmol), and H_2O (0.40 g, 22 mmol) in 10 mL of dry DMF. The combined mixture was stirred for 4 h at rt and diluted with 30 mL of EtOAc. The organic layer was washed with saturated NH_4Cl solution, saturated $NaHCO_3$ solution, water twice, and brine and dried over $MgSO_4$. After filtration and concentration, the crude product was separated by silica gel column chromatography (elution with hexane/EtOAc

= 5:1) to afford 0.820 g of **11** (96%): $[\alpha]^{24}_D = -1.30$ (*c* 1.13, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28−7.34 (m, 5H), 5.82 (s, 2H), 5.07 (s, 2H), 4.52 (bs, 1H), 3.73 (m, 1H), 2.57 (t, J = 4.2 Hz, 2H), 2.53 (t, J = 3.9 Hz, 2H), 1.62 (m, 2H), 1.57 (m, 2H), 1.47 (m, 2H), 1.37 (m, 2H), 1.12 (d, J = 6.5 Hz, 3H), 0.91 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.7, 154.8, 154.7, 136.6, 128.5(3), 128.0(2), 105.2, 104.8, 66.5, 47.0, 36.5, 30.2, 27.8, 27.7, 24.6, 22.2, 21.2, 13.8; IR (neat) 3329, 2932, 1697, 1532 cm^{-1}; mass spectrum (EI) *m*/*z* 343 (M^+); exact mass calcd for $C_{21}H_{29}NO_3$ 343.2147, found 343.2147.

(2*S*)-2-(*N*-Benyloxycarbonylamino)-6,9-dioxo-7-tridecene (2b). To a solution of **11** (0.023 g, 0.067 mmol) in EtOH (0.3 mL) was added MMPP (0.023 g, 0.046 mmol) in water (0.3 mL) at rt. The mixture was stirred at rt for 3 h. Addition of saturated aqueous $NaHCO_3$ solution to the mixture was followed by extraction with 3 mL of CH_2Cl_2 twice. The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by silica gel column chromatography (elution with hexane/EtOAc = 3:1) to provide 0.015 g of **2b** (62% yield): $[\alpha]^{24}_D = 0.8$ (*c* 1.50, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26−7.34 (m, 5H), 6.25 (s, 2H), 5.06 (s, 2H), 4.52 (bd, J = 9.3 Hz, 1H), 3.58 (m, 1H), 2.54 (t, J = 6.9 Hz, 2H), 2.49 (t, J = 7.3 Hz, 2H), 1.61 (m, 2H), 1.46 (m, 2H), 1.38 (m, 2H), 1.35 (m, 2H), 0.89 (t, J = 7.3 Hz, 3H), 0.85 (d, J = 4.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.7 (2), 155.8, 136.6, 136.0, 135.2, 128.5 (3), 128.0 (2), 66.5, 46.8, 42.3, 41.8, 36.1, 25.5, 22.2, 21.2, 19.7, 13.8; IR (neat) 3342, 2958, 1700, 1699, 1527 cm^{-1}; mass spectrum (EI) *m*/*z* 359 (M^+); exact mass calcd for $C_{21}H_{29}NO_4$ 359.4593, found 359.4499.

(+)-Monomorine 1. A 15 mL, one-necked, round-bottomed flask equipped with a rubber septum was charged with a solution of **2a** (30.0 mg, 0.08 mmol) in 5 mL of MeOH containing 10% palladium on activated carbon (2.04 mg, 0.004 mmol). The flask atmosphere was replaced by hydrogen gas via blowing an excess amount of gas, and the solution was stirred under hydrogen balloon at rt for 1 h. The solution was filtered through Celite and concentrated carefully. The crude product was separated by silica gel column chromatography (elution with pentane/ether = 10:1) to afford 7.8 mg of **1** (50%) and 0.6 mg of **11** (4%).

A 15 mL, one-necked, round-bottomed flask equipped with a rubber septum was charged with a solution of **2b** (30.0 mg, 0.08 mmol) in 5 mL of MeOH containing 10% palladium on activated carbon (2.04 mg, 0.004 mmol). The flask atmosphere was replaced by hydrogen gas via blowing an excess amount of gas, and the solution was stirred under hydrogen balloon at rt for 5 h. The solution was filtered through Celite and concentrated carefully. The crude product was separated by silica gel column chromatography (elution with pentane/ether = 10:1) to afford 7.0 mg of **1** (45%) and 0.5 mg of **11** (less than 4%): $[\alpha]^{24}_D = 29.0$ (*c* 0.80, hexane) and 30.2 (*c* 2.05, hexane), respectively [lit.[2a] [α] 35.7 (*c* 0.370, hexane)]; ^{1}H NMR (500 MHz, CD_3OD) δ 2.45−2.51 (m, 1H), 2.19−2.21 (m, 1H), 2.07−2.10 (m, 1H), 1.19−1.94 (m, 16H), 1.15 (d, J = 6.4 Hz, 3H), 0.90 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ 68.8, 65.0, 62.3, 39.7, 36.0, 30.7, 30.6, 30.5, 30.3, 25.5, 23.9, 22.9, 14.5; mass spectrum (EI) *m*/*z* 195 (M^+); exact mass calcd for $C_{13}H_{25}N$ 195.1987, found 195.1970.

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Supporting Information Available: Copies of ^{1}H NMR spectra of **4**, **7**, and **9** and ^{1}H and ^{13}C NMR spectra of **2a**,**b**, **3**, **5**, **10**, and **12**. This material is available free of charge via the Internet at http://pubs.acs.org.

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