JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

Total Synthesis of (−)-Sessilifoliamide J

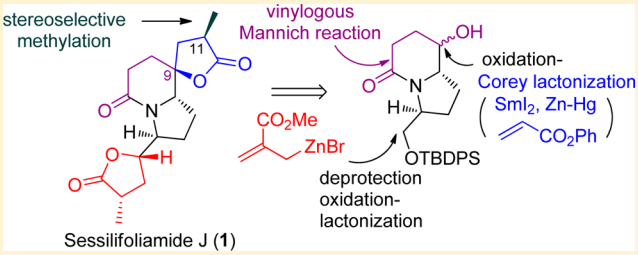
Xue-Kui Liu,[†] Jian-Liang Ye,[†] Yuan-Ping Ruan,[†] Yu-Xiu Li,[†] and Pei-Qiang Huang*[,†,‡]

[†]Department of Chemistry, College of Chemistry and Chemical Engineering, Xiamen University, Xiamen, Fujian 361005, P. R. China

[‡]State Key Laboratory of Bioorganic and Natural Products Chemistry, 354 Fenglin Lu, Shanghai 200032, P. R. China

Supporting Information

ABSTRACT: An efficient synthesis of the *Stemona* alkaloid (−)-sessilifoliamide J (**1**) in 12 steps and 7.7% overall yield from the known building block **8** is presented. The synthesis features the Corey lactonization reaction and a highly diastereoselective α-methylation reaction to build the spirolactone moiety.



INTRODUCTION

Over one hundred alkaloids have been isolated from plants of genus *Stemona* (family Stemonaceae).[1] The extracts of roots and leaves of *Stemonaceae* plants have been used in China and Japan for centuries as cough suppressants and domestic insecticides.[2] Recent studies showed that some of them possess interesting bioactivities.[3] The diverse and challenging structures of *Stemona* alkaloids serve as attractive targets for synthetic organic chemists, and in turn resulted in a number of elegant total syntheses in either racemic or enantioselective manners. Many novel and efficient synthetic strategies were thus developed.[4−12] Sessilifoliamide J (**1**) (Figure 1) is a *Stemona* alkaloid isolated in 2008 from the roots of *Stemona sessilifolia* (Miq.) Miq. (Stemonaceae).[13] Its structure and relative stereochemistry was established by single crystal X-ray crystallography analysis. The absolute configuration of the natural product was determined very recently by our group as 3*S*,9*S*,9*aS*,11*R*,14*S*,16*S*.[14]

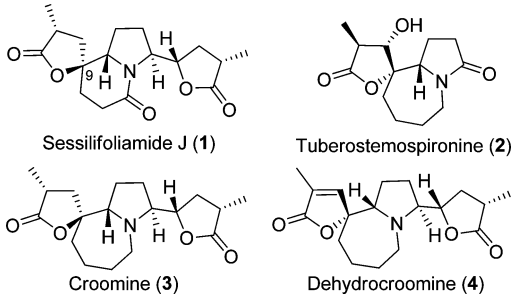


Figure 1. Structures of (−)-sessilifoliamide J (**1**) and some tuberostemospironine group alkaloids.

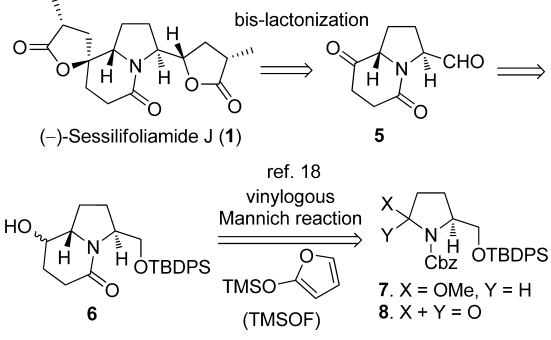
Structurally, sessilifoliamide J (**1**) contains a six-membered piperidin-2-one ring, which is unique among the known *Stemona* alkaloids; the C9 spiro α-methyl-γ-lactone moiety also found in tuberostemospironine subclass of *Stemona* alkaloids, such as tuberostemospironine (**2**), croomine (**3**), and dehydrocroomine (**4**).

As a continuation of a program directed toward the total synthesis of alkaloids,[15] we have embarked recently on the total synthesis of sessilifoliamide J (**1**).[14] Our previous synthetic efforts have led to the synthesis of 9-*epi*-sessilifoliamide J along with sessilifoliamide J (**1**) as a minor diastereomer.[14] However, an efficient total synthesis of sessilifoliamide J (**1**) has not yet been achieved. Toward this end, and in light of our previous results,[14] we devised an alternative approach starting from the known chiron **8**. We now report the successful implementation of this new approach, which resulted in an efficient synthesis of sessilifoliamide J (**1**).

RESULTS AND DISCUSSION

Our initial retrosynthetic analysis of sessilifoliamide J (**1**) is outlined in Scheme 1. The retro-bis-lactonization[16] disconnection implicates ketoaldehyde **5** as the key intermediate. The

Scheme 1. Retrosynthetic Analysis of (−)-Sessilifoliamide J



Special Issue: Robert Ireland Memorial Issue

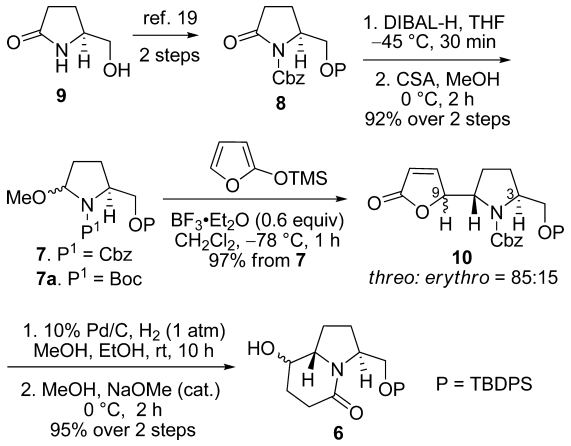
Received: July 13, 2012

   dx.doi.org/10.1021/jo3014484 | J. Org. Chem. XXXX, XXX, XXX−XXX

subsequent retro-vinylogous Mannich reaction (VMR)[17] disconnection has been well documented.[18−20] The challenges associated with the synthetic route based on this retrosynthetic analysis include the unprecedented one-pot bis-lactonization and the establishment of the four new chiral centers with correct stereochemistries.

Our investigation started with the construction of the indolizidinone skeleton **6**. Although the synthesis of this compound has been reported previously by Hanessian[18a] and Rassu/Casiraghi,[18b] respectively, starting from the *N,O*-acetal **7a**,[18] we devised a modified three-step approach to **6** involving the use of Cbz-protected *N,O*-acetal **7**[19] in a VMR (Scheme 2).

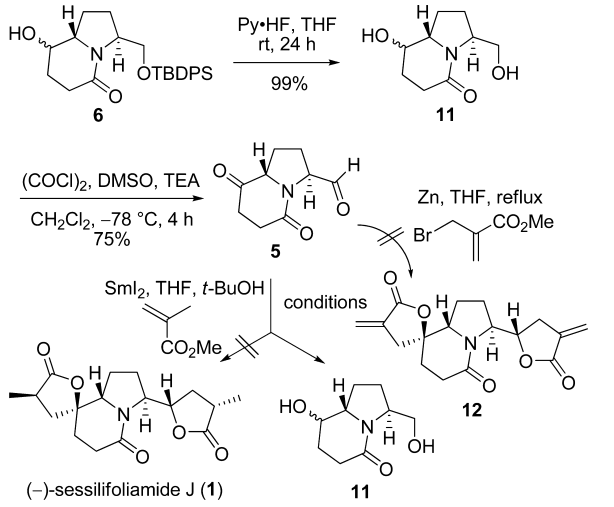
Scheme 2. Synthesis of the Indolizidinone Skeleton 6



Thus, compound **8**, easily obtained from commercially available (*S*)-pyroglutaminol **9** as described by Martin et al.,[19] was subjected to successive partial reduction with DIBAL-H and CSA-catalyzed reaction with MeOH to afford the known *N,O*-acetal **7**[19] in 92% overall yield. The $BF_3{\cdot}Et_2O$-catalyzed VMR[18] between **7** and (trimethylsiloxy)furan (TMSOF) at −78 °C in CH_2Cl_2 for 1 h produced an 85:15 ratio (determined by HPLC on a crude) of *threo*-**10** and its *erythro* diastereomer in 97% yield (Scheme 2). According to our synthetic plan, both diastereomers can be used for the synthesis of the target molecule. Thus, under catalytic hydrogenation conditions (10% Pd/C, H_2 1 atm, 10 h), the diastereomeric mixture of **10** was converted into the *N*-deprotected pyrrolidine-lactone. The resulting lactone−pyrrolidine, without purification, was treated with a catalytic amount of NaOMe at 0 °C for 2 h to afford indolizidinone **6** as a diastereomeric mixture in 95% yield over two steps.

To prepare the ketoaldehyde **5** according to the planned bis-lactonization, indolizidinone **6** was treated with 10 equiv of Py·HF adduct in THF at room temperature for 24 h, which gave the diol **11** in practically quantitative yield (Scheme 3). The bis-oxidation of the diol **11** was attempted with several methods including the Ley oxidation, Dess−Martin oxidation, and Parikh−Doering oxidation. Even though the desired bis-oxidation reaction took place under the above-mentioned conditions, partial epimerization was observed. Only the Swern oxidation at −78 °C afforded the desired ketoaldehyde **5** in a 75% yield. This ketoaldehyde turned out to be very susceptible to epimerization, which could occur during the purification by column chromatography on silica gel or when stored at 4 °C for several hours.

Scheme 3. Attempted Bis-lactonization Approach

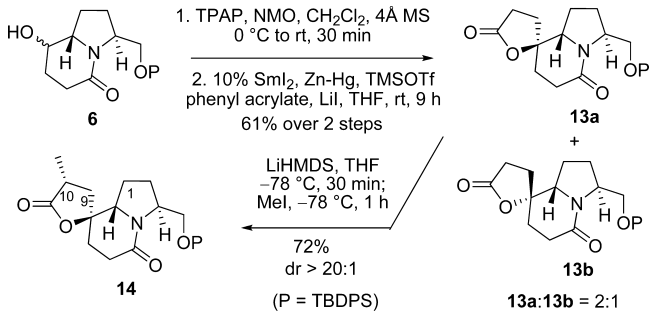


Due to the configurational instability of the chiral aldehyde, the crude ketoaldehyde **5** was promptly subjected to the SmI_2-mediated bis-lactonization. Although many SmI_2-mediated lactonization reactions between ketones and activated alkenes have been reported,[21] our attempts of various lactonization conditions[22] yielded neither the bis-lactonization of the ketoaldehyde **5** to methyl methacrylate nor the monolactonization of the aldehyde group apart from the reduced product **11**.

We next tried the Reformatsky-type reaction[23] by treating ketoaldehyde **5** with organozinc reagent generated in situ from zinc and methyl bromomethacrylate in THF at reflux. Unfortunately, none of the desired product **12** was observed. Instead, a rapid degradation of the starting ketoaldehyde in refluxing THF was observed. At this stage, we decided to abandon the initial plan of the one-pot bis-lactonization. A stepwise installation of the two lactone rings in (−)-sessilifoliamide J (**1**) was anticipated.

We next proceeded to investigate the stepwise oxidation−spiro-lactonization of alcohol **6** (Scheme 4). In contrast to the

Scheme 4. Stereoselective Installation of the Spiro-Lactone Moiety



bis-oxidation of diol **11**, oxidation of the alcohol **6** under either Ley or Dess−Martin oxidation conditions proceeded smoothly to give the corresponding ketone. However, partial epimerization at C8a was observed once again during the column chromatography purification. This could be avoided by subjecting the crude ketone directly to the SmI_2-mediated lactonization reaction with methyl methacrylate. In view of our previous results,[14] it was obvious that the conditions we used previously for the spiro-lactonization at C8 would lead to 9-*epi*-

dx.doi.org/10.1021/jo3014484 | J. Org. Chem. XXXX, XXX, XXX−XXX

sessilifoliamide J.[24] To install the correct stereochemisry at C8 in sessilifoliamide J (**1**), we turned to the lactonization method reported by Corey and Zheng.[25] Indeed, the Ley oxidation–Corey lactonization (10% SmI_2, LiI, Zn–Hg, phenyl acrylate, TMSOTf, THF, rt) of the alcohol **6** produced lactone **13** (Scheme 4) as a separable diastereomeric mixture in a ratio of 2:1 (**13a**:**13b**) in favor of the desired diastereomer **13a**. Their stereochemistries were deduced from that of compound **14**. Remarkably, the α-methylation (LiHMDS, THF, −78 °C, then MeI) of lactone **13a** gave almost exclusively the (8*S*,10*R*)-diastereomer **14** in 72% yield. The relative stereochemistry of compound **14** was determined by NOESY experiments. The observed NOESY correlations (cf. Supporting Information for the NOESY spectrum) between $H_{7\beta} \leftrightarrow H_{8a}$, $H_{8a} \leftrightarrow H_{1\beta} \leftrightarrow CH_2OTBDPS$ and those between $H_{7\alpha} \leftrightarrow H_{9\beta} \leftrightarrow$ 10-Me (Figure 2) allowed the unambiguous assignment of the stereochemistry for compound **14**.

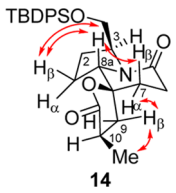
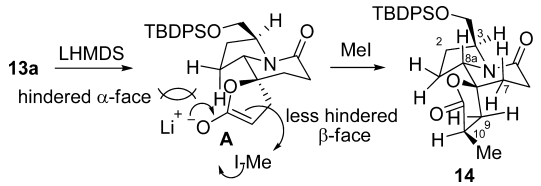


Figure 2. Key correlations observed from the NOESY spectrum of compound **14**.

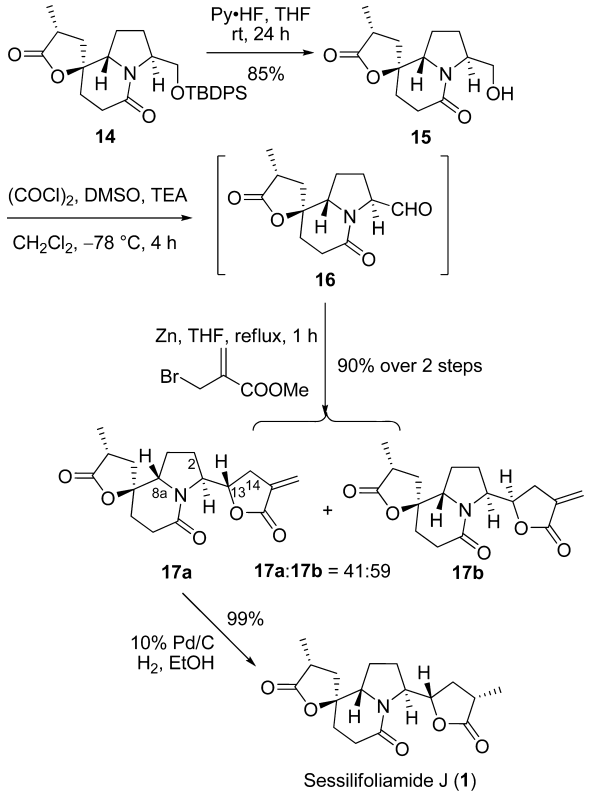
It is worth noting that although methylation is a valuable tactic frequently used for the construction of the α-methyllactone moiety of *Stemona* alkaloids,[4,5e,f,8b] it has not been used for the α-methylation of the spirolactone to the best of our knowledge. The stereochemical outcome of the highly diastereoselective methylation of the enolate (**A**) generated from the diastereomer **13a** can be understood on the basis of the conformation of the enolate **A**. The α-face (concave) of the enolate, being blocked by the indolizidinone moiety, is highly hindered. The approach of the electrophile (methyl iodide) from the β-face (convex) predominates, giving rise to the methylated product **14** with a *R*-configuration at the newly formed stereogenic center.

Scheme 5. Stereochemical Course of the Highly Diastereoselective Methylation



The remaining task for our total synthesis of sessilifoliamide J (**1**) was the construction of the second lactone ring. For this purpose, compound **14** was desilylated (10 equiv Py·HF, THF, rt) to give the corresponding compound **15** in 85% yield (Scheme 6). The Swern oxidation of alcohol **15** proceeded smoothly to produce aldehyde **16**. However, epimerization of **16** occurred during its purification by column chromatography on silica gel. This prompted us to attempt a tandem protocol. While the tandem oxidation–SmI_2-mediated lactonization was unsuccessful, oxidation followed by organozinc reagent addition[23] led, without observable racemization, to the

Scheme 6. Synthesis of (−)-Sessilifoliamide J



diastereomeric lactones **17a** and **17b** in a 41:59 ratio (determined by HPLC on a crude) with a combined yield of 90% from compound **15**. The stereochemical assignment for **17a** was confirmed by the ultimate transformation of **17a** into (−)-sessilifoliamide J, while that of **17b** could be deduced from **17a**. Hydrogenation[6c] [10% Pd/C, EtOH, H_2 (1 atm), rt] of the diastereomer **17a** produced (−)-sessilifoliamide J (**1**) as the sole diastereomer in 99% yield. The specific optical rotation data [synthetic **1**: $[\alpha]^{20}_D$ −72 (*c* 0.15, $CHCl_3$); natural sessilifoliamide J (**1**): $[\alpha]^{26}_D$ −73 (*c* 0.13, $CHCl_3$);[13] previous synthesized compound: $[\alpha]^{20}_D$ −71 (*c* 0.15, $CHCl_3$)[14]] and spectroscopic data of our synthetic material are in agreement with those reported previously.[13]

CONCLUSIONS

In summary, we accomplished the first total synthesis of the natural (−)-sessilifoliamide J (**1**) in 12 steps with an overall yield of 7.7% starting from the known building block **8** (14 steps and 6.7% overall yield from commercially available **9**). Through this work, we demonstrated that the Corey lactonization method is useful for the stereoselective construction of the spiro-lactone moiety of the *Stemona* alkaloid, and the subsequent lactone α-methylation can be achieved with excellent diastereoselectivity.

EXPERIMENTAL SECTION

General Methods. Melting points were uncorrected. Infrared spectra were measured using film KBr pellet techniques. ^1H NMR spectra were recorded in $CDCl_3$ with tetramethylsilane as an internal standard. Chemical shifts are expressed in δ (ppm) units downfield from TMS. Silica gel (300–400 mesh) was used for flash column chromatography, eluting (unless otherwise stated) with ethyl acetate/hexane. Ether and THF were distilled over sodium benzophenone ketyl under N_2. Dichloromethane was distilled over calcium hydride

dx.doi.org/10.1021/jo3014484 | J. Org. Chem. XXXX, XXX, XXX–XXX

under N_2. High-resolution mass spectra were obtained using electrospray ionization using an ICR analyzer (ESI-MS).

Benzyl (2*S*,5*R/S*)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-5-methoxypyrrolidine-1-carboxylate (7). To a solution of the known chiron **8**[19] (6.10 g, 12.5 mmol) in anhydride THF (125 mL) was added dropwise a solution of DIBAL-H (1 M in hexane, 13.7 mL, 13.7 mmol) at −45 °C under N_2. After being stirred at the same temperature for 30 min, the reaction was quenched with a saturated aqueous NH_4Cl (5 mL) and a 1 M HCl (30 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was dissolved in MeOH (125 mL), and camphorsulfonic acid (CSA, 360 mg, 1.3 mmol) was added at 0 °C. After being stirred at 0 °C for 2 h, the reaction was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel eluting with EtOAc/hexane (1:8) to afford the known compound **7**[19](5.80 g, yield: 92%) as an inseparable diastereomeric mixture whose diastereomeric ratio was not determined due to the rotamerism. Compound **7**: colorless oil. Data of the diastereomeric mixture: IR (film) ν_{max} 3070, 3044, 2931, 2857, 1776, 1708, 1643, 1470, 1402, 1356, 1166, 1112 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.05 and 1.07 (2s, 9H), 1.74−1.88 (m, 1H), 1.90−2.08 (m, 1H), 2.10−2.30 (m, 2H), 3.18−3.46 (m, 3H), 3.50−4.15 (m, 3H), 4.94−5.36 (m, 3H), 7.10−7.46 (m, 11H), 7.60−7.76 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.2 and 19.3 (C), 25.2 and 25.9 (CH_2), 26.86 and 26.92 (CH_3), 29.4 (CH_2), 30.4 (CH_2), 31.5 (CH_2), 35.2 (CH_2), 55.6 and 56.6 (CH_3), 58.3 and 58.8 (CH), 63.6 and 64.1 (CH_2), 66.8, 66.9, and 67.1 (CH_2), 89.9 and 90.4 (CH), 127.6(CH), 127.7 (CH), 128.0 (CH), 128.1 (CH), 128.4 (CH), 128.5 (CH), 133.6 (C), 133.8 (C), 134.8 (C), 135.6 (CH), 136.4 (C), 154.9 (CO); HRMS (ESI) calcd for $[C_{30}H_{37}NO_4Si + Na^+]$ 526.2284, found 526.2284.

Benzyl (2*S*,5*S*)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-5-(5-oxo-2,5-dihydrofuran-2-yl)pyrrolidine-1-carboxylate (10). To a cooled solution (−78 °C) of compound **7** (2.178 g, 4.33 mmol) in anhydrous CH_2Cl_2 (43 mL) was added dropwise (trimethylsiloxy)-furan (TMSOF, 1.09 mL, 6.50 mmol) under N_2. After being stirred at −78 °C for 15 min, $BF_3{\cdot}Et_2O$ (0.32 mL, 2.60 mmol) was added dropwise. After being stirred for an additional 1 h at the same temperature, the reaction was quenched with a saturated aqueous $NaHCO_3$ (10 mL). The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel eluting with EtOAc/hexane (1:4) to afford compound **10** (2.320 g, yield: 97%) as an inseparable diastereomeric mixture in a ratio of 85:15 [determined by HPLC: Shim-pack VP-ODS (150 × 4.6), CH_3CN/H_2O 75:25, 1.2 mL/min, λ = 254 nm, t_1 = 79.8 min (85.4%), t_2 = 86.4 min (14.6%)]. Compound **10**: colorless oil. Data of the diastereomeric mixture: IR (film) ν_{max} 3070, 2957, 2930, 2857, 1759, 1698, 1405, 1354, 1157, 1112 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.019, 1.025, and 1.035 (3s, 9H), 1.43−1.56 and 1.65−1.72 (m, 1H), 1.78−2.10 (m, 2H), 2.14−2.30 (m, 1H), 3.58−3.75 and 3.90−4.22 (m, 3H), 4.44 (dd, J = 8.6, 3.5 Hz, 0.8H) and 4.89 (t, J = 1.8 Hz, 0.2H), 4.82 (d, J = 12.2 Hz, 0.6H) and 4.91−5.21 (m, 1.4H), 5.30−5.80 (m, 1H), 5.92−6.18 (m, 1H), 7.00−7.70 (m, 16H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.1 and 19.2 (C), 24.87 and 24.94 (CH_2), 26.8 and 26.9 (CH_3), 27.2 and 27.8 (CH_2), 58.4 and 58.9 (CH), 59.6 and 60.2 (CH), 63.3, 64.3, and 64.5 (CH_2), 67.1, 67.3, and 72.0 (CH_2), 83.9 (CH), 121.0 and 122.4 (CH), 127.1 (CH), 127.8 (CH), 128.0 (CH), 128.1 (CH), 128.3 (CH), 128.4 (CH), 128.7 (CH), 129.75 (CH), 129.80 (CH), 129.83 (CH), 133.2 (C), 133.3 (C), 133.4 (C), 135.5 and 136.6 (CH), 136.1 (CH), 153.4 (CH), 153.7 (CH), 154.2 (CH), 154.7 (CH), 172.4 and 172.9 (CO); HRMS (ESI) calcd for $[C_{33}H_{37}NO_5Si + Na^+]$ 578.2333, found 578.2334.

(3*S*,8a*S*)-3-((*tert*-Butyldiphenylsilyloxy)methyl)-8-hydroxy-hexahydroindolizin-5(1*H*)-one (6). A suspension of 10% Pd on carbon (232 mg) and **10** (2.32 g, 4.20 mmol) in MeOH (42 mL) was stirred under H_2 (1 atm) for 10 h. The mixture was filtered through Celite, and the retained solids were washed with MeOH (7 × 10 mL). To the combined filtrates was added NaOMe (45 mg, 0.84 mmol) at 0 °C. After being stirred at 0 °C for 2 h, the reaction was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel eluting with EtOAc to afford compound **6** (1.68 g, yield: 95%) as an inseparable diastereomeric mixture. Compound **6**: colorless oil; IR (film) ν_{max} 3483, 3285, 3070, 3046, 2961, 2928, 2875, 2853, 1622, 1606, 1470, 1426, 1413, 1315, 1112, 1093, 1072 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) data of the major diastereomer read from the spectrum of the mixture δ 1.05 (s, 9H), 1.72−1.81 (m, 1H), 1.85−2.10 (m, 5H), 2.20−2.35 (m, 1H), 2.46 (ddd, J = 18.8, 12.2, 7.1 Hz, 1H), 2.72 (br s, 1H), 3.60 (td, J = 8.4, 2.4 Hz, 1H), 3.75 (dd, J = 10.1, 2.4 Hz, 1H), 4.04 (br s, 1H), 4.07 (dd, J = 10.1, 4.2 Hz, 1H), 4.18−4.25 (m, 1H), 7.34−7.44 (m, 6H), 7.58−7.65 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) data of the major diastereomer read from the spectrum of the mixture δ 19.4 (C), 24.5 (CH_2), 26.3 (CH_2), 26.7 (CH_2), 26.9 (CH_3), 28.2 (CH_2), 58.2 (CH), 63.4 (CH), 63.7 (CH), 64.2 (CH_2), 127.63 (CH), 127.65 (CH), 129.6 (CH), 129.7 (CH), 133.7 (C), 135.5 (CH), 135.6 (CH), 168.6 (CO); HRMS (ESI) calcd for $[C_{25}H_{33}NO_3Si + Na^+]$ 446.2122, found 446.2121.

(3*S*,8a*S*)-8-Hydroxy-3-(hydroxymethyl)hexahydroindolizin-5(1*H*)-one (11). To a cooled solution (0 °C) of compound **6** (210 mg, 0.50 mmol) in anhydrous THF (5 mL) was added Py·HF (0.45 mL, 5.0 mmol) dropwise under N_2. After being stirred at room temperature for 24 h, the mixture was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel eluting with EtOAc/MeOH (15:1) to afford compound **11** (92 mg, yield: 99%) as an inseparable diastereomeric mixture. Compound **11**: white solid; IR (film) ν_{max} 3485, 3415, 3280, 2960, 2928, 2874, 2853, 1620, 1600, 1470, 1425, 1112, 1093 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) data of the major diastereomer read from the spectrum of the mixture δ 1.60−1.94 (m, 4H), 2.01−2.15 (m, 2H), 2.37 (dd, J = 18.2, 7.0 Hz, 1H), 2.54 (ddd, J = 18.2, 12.4, 7.2 Hz, 1H), 3.46−3.56 (m, 2H), 3.65 (app d, J = 11.3 Hz, 1H), 4.06−4.21 (m, 2H), 5.65 and 5.94 (br 2s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) data of the major diastereomer read from the spectrum of the mixture δ 26.0 (CH_2), 26.2 (CH_2), 26.3 (CH_2), 27.9 (CH_2), 61.9 (CH), 63.0 (CH), 63.5 (CH), 67.5 (CH_2), 172.0 (CO); HRMS (ESI) calcd for $[C_9H_{15}NO_3 + Na^+]$ 208.0944, found 208.0946.

(3*S*,8a*S*)-5,8-Dioxooctahydroindolizine-3-carbaldehyde (5). To a cooled solution of $(COCl)_2$ (0.40 mL, 4.20 mmol) in anhydrous CH_2Cl_2 (7 mL) was added DMSO (0.35 mL, 4.90 mmol) in anhydrous CH_2Cl_2 (2 mL) at −78 °C over 30 min. After being stirred at −78 °C for another 30 min, to the resulting mixture was slowly added diol **11** (130 mg, 0.70 mmol) in anhydrous CH_2Cl_2 (2 mL) at −78 °C over 30 min. After being stirred at −78 °C for an additional 1 h, to the solution was slowly added TEA (1.17 mL, 8.40 mmol) at −78 °C over 30 min. After being stirred at the same temperature for 2 h, the reaction was quenched with H_2O (2 mL). The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 2 mL). The combined organic layers were washed with brine (1 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford crude ketoaldehyde **5** (96 mg, yield: 75%) as a pale yellow oil: IR (film) ν_{max} 2917, 2845, 2776, 1765, 1735, 1715, 1464, 1389, 1335, 1130, 1066 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.94−2.01 (m, 1H), 2.00−2.21 (m, 2H), 2.23−2.30 (m, 1H), 2.54−2.65 (m, 1H), 2.67−2.78 (m, 2H), 2.83−2.95 (m, 1H), 4.20 (t, J = 7.4 Hz, 1H), 4.66 (t, J = 7.0 Hz, 1H), 9.61 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 23.9 (CH_2), 26.9 (CH_2), 30.5 (CH_2), 34.5 (CH_2), 64.7 (CH), 65.1 (CH), 169.2 (CO), 197.7 (CHO), 205.8 (CO); HRMS (ESI) calcd for $[C_9H_{11}NO_3 + Na^+]$ 204.0631, found 204.0628.

Synthesis of Compounds 13a and 13b by Ley Oxidation−Corey Lactonization Reaction (2*S*,3′*S*,8a′*S*)-3′-((*tert*-Butyldiphenylsilyloxy)methyl)tetrahydro-1′*H*,3*H*-spiro[furan-2,8′-indolizine]-5,5′(4*H*,8a′*H*)-dione (13a) (2*R*,3′*S*,8a′*S*)-3′-((*tert*-Butyldiphenylsilyloxy)methyl)tetrahydro-1′*H*,3*H*-spiro-[furan-2,8′-indolizine]-5,5′(4*H*,8a′*H*)-dione (13b). To a solution of compound **6** (423 mg, 1.0 mmol) in CH_2Cl_2 (10 mL) were added 4 Å molecular sieves (423 mg), NMO (293 mg, 2.5 mmol), and TPAP

dx.doi.org/10.1021/jo3014484 | J. Org. Chem. XXXX, XXX, XXX−XXX

(35 mg, 0.1 mmol). The resultant mixture was stirred at room temperature for 30 min before being filtered through a thin silica gel pad eluting with EtOAc/hexane (1:1). The solvent was removed under reduced pressure. The crude ketone was used in the next step without further purification. A suspension of LiI (700 mg, 5.20 mmol), the crude ketone (1.0 mmol), and phenyl acrylate (0.166 mL, 1.2 mmol) in THF (5 mL) was placed in a 5 mL gastight syringe which was mounted on a syringe drive. A small aliquot of the solution (0.5 mL) was added to a mixture of Zn−Hg (1 g, 15 mmol) and SmI_2 (0.1 M, 1.0 mL, 0.1 mmol) in THF (15 mL) at room temperature. The rest of the solution was added by the drive over 9 h. The reaction mixture changed color gradually from dark blue to light blue. A small portion of TMSOTf (10 μL, 0.06 mmol) was then added via a 100 μL gastight micro syringe as soon as the color of the reaction mixture faded to light blue. The reaction mixture became dark blue again in less than 2 min. When the color faded to light blue, a second aliquot of TMSOTf (10 μL, 0.06 mmol) was added to restore the dark blue color. TMSOTf was added portionwise as described above until the reaction was judged completed by TLC monitoring. The total amount of TMSOTf used was about 550 μL (3.0 mmol), and the total time of reaction was about 9 h. The reaction mixture was concentrated in vacuo to remove THF, treated with saturated aqueous $NaHCO_3$ (10 mL) and extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with brine (1 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel eluting with EtOAc/hexane (2:1) to afford diastereomers **13a** (194 mg, yield: 41%) and **13b** (97 mg, yield: 20%).

Compound **13a**: colorless oil; $[\alpha]^{20}_D$ −33.8 (*c* 1.0, $CHCl_3$); IR (film) ν_{max} 3070, 3046, 2930, 2856, 1777, 1656, 1643, 1427, 1413, 1113, 1068, 1018 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.06 (s, 9H), 1.41−1.53 (m, 1H), 1.88−2.04 (m, 3H), 2.05−2.21 (m, 4H), 2.33 (ddd, *J* = 18.5, 11.7, 6.8 Hz, 1H), 2.50−2.71 (m, 3H), 3.72 (dd, *J* = 10.2, 2.4 Hz, 1H), 3.86 (dd, *J* = 10.5, 5.2 Hz, 1H), 4.12 (dd, *J* = 10.2, 4.0 Hz, 1H), 4.18−4.26 (m, 1H), 7.34−7.44 (m, 6H), 7.58−7.61 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.3 (C), 24.5 (CH_2), 25.6 (CH_2), 26.8 (CH_2), 26.9 (CH_3), 28.6 (CH_2), 28.8 (CH_2), 33.2 (CH_2), 58.7 (CH), 63.6 (CH_2), 64.6 (CH), 83.7 (C), 127.7 (CH), 129.8 (CH), 133.3 (C), 133.4 (C), 135.5 (CH), 135.6 (CH), 166.8 (CO), 175.2 (CO); HRMS (ESI) calcd for $[C_{28}H_{35}NO_4Si + Na^+]$ 500.2228, found 500.2234.

Compound **13b**: colorless oil; $[\alpha]^{20}_D$ −62.8 (*c* 1.0, $CHCl_3$); IR (film) ν_{max} 3070, 3044, 2955, 2930, 2857, 1779, 1641, 1461, 1427, 1411, 1193, 1112, 1028 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.06 (s, 9H), 1.72 (m, 1H), 1.83 (m, 1H), 1.91−1.98 (m, 1H), 2.00−2.11 (m, 4H), 2.12−2.18 (m, 1H), 2.37 (dd, *J* = 17.3, 6.2 Hz, 1H), 2.48−2.72 (m, 3H), 3.66 (dd, *J* = 11.0, 5.4 Hz, 1H), 3.76 (dd, *J* = 10.2, 2.3 Hz, 1H), 4.16 (dd, *J* = 10.2, 3.9 Hz, 1H), 4.24−4.30 (m, 1H), 7.34−7.44 (m, 6H), 7.59−7.62 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.4 (C), 23.9 (CH_2), 25.5 (CH_2), 26.9 (CH_3), 28.0 (CH_2), 28.2 (CH_2), 30.1 (CH_2), 32.9 (CH_2), 58.3 (CH), 64.3 (CH_2), 65.8 (CH), 81.7 (C), 127.68 (CH), 127.70 (CH), 129.7 (CH), 129.8 (CH), 133.5 (C), 133.6 (C), 135.49 (CH), 135.53 (CH), 167.1 (CO), 175.6 (CO); HRMS (ESI) calcd for $[C_{28}H_{35}NO_4Si + Na^+]$ 500.2228, found 500.2228.

(2*S*,3″*S*,4*R*,8a′*S*)-3′-((*tert*-Butyldiphenylsilyloxy)methyl)-4-methyltetrahydro-1′*H*,3*H*-spiro[furan-2,8′-indolizine]-5,5′(4*H*,8a′*H*)-dione (14). To a solution of lactone **13a** (400 mg, 0.84 mmol) in THF (8.5 mL) was added LiHMDS (0.872 mL, 0.924 mmol, 1.06 M in THF/ethylbenzene) at −78 °C under N_2. After the solution was stirred at −78 °C for 30 min, MeI (0.26 mL, 4.20 mmol) was added and stirring continued for 1 h at −78 °C. The reaction was quenched with saturated NH_4Cl (0.5 mL), and the resulting mixture was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel eluting with EtOAc to afford compound **17** (296 mg, yield: 72%) as a white solid: mp 78−81 °C (EtOAc); $[\alpha]^{20}_D$ −35.0 (*c* 0.9, $CHCl_3$); IR (film) ν_{max} 3075, 3041, 2917, 2849, 1777, 1657, 1642, 1427, 1383, 1284, 1113, 1019 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.05 (s, 9H), 1.31 (d, *J* = 7.1 Hz, 3H), 1.37−1.50 (m, 1H), 1.60 (dd, *J* = 13.4, 10.8 Hz, 1H), 1.85 (ddd, *J* = 12.6, 6.3, 1.8 Hz, 1H), 1.99−2.13 (m, 3H), 2.20 (td, *J* = 12.6, 6.4 Hz, 1H), 2.32 (ddd, *J* = 18.2, 12.6, 6.2 Hz, 1H), 2.43−2.56 (m, 2H), 2.67−2.79 (m, 1H), 3.71 (dd, *J* = 10.1, 1.9 Hz, 1H), 3.81 (dd, *J* = 11.2, 4.8 Hz, 1H), 4.15 (dd, *J* = 10.1, 7.4 Hz, 1H), 4.15−4.20 (m, 1H), 7.34−7.44 (m, 6H), 7.58−7.62 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.7 (CH_3), 19.3 (C), 24.4 (CH_2), 26.9 (CH_3), 27.3 (CH_2), 28.7 (CH_2), 34.6 (CH_2), 35.0 (CH_2), 35.3 (CH), 58.6 (CH), 63.4 (CH_2), 64.9 (CH), 81.4 (C), 127.7 (CH), 129.8 (CH), 133.4 (C), 133.5 (C), 135.5 (CH), 135.6 (CH), 166.8 (CO), 178.0 (CO); HRMS (ESI) calcd for $[C_{29}H_{37}NO_4Si + Na^+]$ 514.2384, found 514.2388.

(2*S*,3′*S*,4*R*,8a′*S*)-3′-(Hydroxymethyl)-4-methyltetrahydro-1′*H*,3*H*-spiro[furan-2,8′-indolizine]-5,5′(4*H*,8a′*H*)-dione (15). To a cooled solution (0 °C) of compound **14** (41 mg, 0.08 mmol) in anhydrous THF (1 mL) under N_2 was added Py·HF (0.072 mL, 0.8 mmol) dropwise. After being stirred at room temperature for 24 h, the mixture was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel eluting with EtOAc/MeOH (15:1) to afford compound **15** (18 mg, yield: 85%) as a white solid: mp 156−158 °C (MeOH); $[\alpha]^{20}_D$ −23.4 (*c* 0.5, $CHCl_3$); IR (film) ν_{max}: 3407, 2917, 2849, 1767, 1620, 1452, 1382, 1215, 1070 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.34 (d, *J* = 7.2 Hz, 3H), 1.41−1.51 (m, 2H), 1.66 (dd, *J* = 13.5, 10.8 Hz, 1H), 1.93 (ddd, *J* = 12.5, 6.2, 1.6 Hz, 1H), 1.99−2.06 (m, 1H), 2.13−2.22 (m, 1H), 2.33 (td, *J* = 12.6, 6.2 Hz, 1H), 2.44 (ddd, *J* = 18.4, 12.6, 6.6 Hz, 1H), 2.51 (dd, *J* = 13.6, 9.9 Hz, 1H), 2.68−2.80 (m, 2H), 3.60 (dd, *J* = 11.4, 7.5 Hz, 1H), 3.72 (br, 1H), 3.76 (td, *J* = 11.4, 4.8 Hz, 1H), 4.18 (app q, *J* = 7.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.6 (CH_3), 25.9 (CH_2), 26.8 (CH_2), 28.6 (CH_2), 34.2 (CH_2), 35.0 (CH_2), 35.2 (CH), 62.4 (CH), 64.6 (CH), 66.9 (CH_2), 81.0 (C), 169.7 (CO), 177.6 (CO); HRMS (ESI) calcd for $[C_{13}H_{19}NO_4 + Na^+]$: 276.1206; found: 276.1211.

Synthesis of Compounds 17a and 17b by Swern Oxidation−organozinc Reagent Addition. (2*S*,3′*S*,4*R*,8a′*S*)-4-Methyl-3′-((*S*)-4-methylene-5-oxotetrahydrofuran-2-yl)tetrahydro-1′*H*,3*H*-spiro[furan-2,8′-indolizine]-5,5′(4*H*,8a′*H*)-dione (17a) and (2*S*,3′*S*,4*R*,8a′*S*)-4-Methyl-3′-((*R*)-4-methylene-5-oxotetrahydrofuran-2-yl)tetrahydro-1′*H*,3*H*-spiro[furan-2,8′-indolizine]-5,5′(4*H*,8a′*H*)-dione (17b). To a cooled solution of $(COCl)_2$ (0.09 mL, 0.96 mmol) in anhydrous CH_2Cl_2 (1 mL) was slowly added DMSO (0.09 mL, 1.28 mmol) in anhydrous CH_2Cl_2 (1 mL) at −78 °C over 30 min. After being stirred at −78 °C for another 30 min, to the reaction was slowly added compound **15** (80 mg, 0.32 mmol) in anhydrous CH_2Cl_2 (2 mL) at −78 °C over 30 min. After being stirred at −78 °C for an additional 1 h, to the solution was slowly added TEA (0.25 mL, 1.92 mmol) at −78 °C over 30 min. After being stirred at the same temperature for 2 h, the reaction was quenched with H_2O (2 mL). The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 2 mL). The combined organic layers were washed with brine (1 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford crude compound **16** as a pale yellow solid, which was used in the next step without further purification. To a stirred solution of aldehyde **16** (79 mg, 0.32 mmol) in dry THF (3 mL) under N_2 atmosphere, Zn (83 mg, 1.28 mmol) was added. The solution was heated, and when reflux started, a solution of ethyl 2-(bromomethyl)acrylate (0.077 mL, 0.64 mmol) in dry THF (1 mL) was added. After 1 h, TLC analysis of the reaction mixture revealed the disappearance of the starting aldehyde. The reaction mixture was filtered through Celite and the solvent was evaporated under vacuum. The remaining colorless oil was purified by preparative HPLC on reversed phase [separated by HPLC: Shim-pack VP-ODS (150 × 15), CH_3CN/H_2O 75:25, 20 mL/min, λ = 254 nm, t_1 = 13.4 min (41.2%), t_2 = 15.6 min (58.8%)] to afford compound **17a** (38 mg, yield: 37%) and compound **17b** (54 mg, yield: 53%). Compound **17a**: white solid; mp 188−190 °C (MeOH); $[\alpha]^{20}_D$ −74.0 (*c* 0.5, $CHCl_3$); IR (film) ν_{max} 2918, 1768, 1654, 1443, 1413, 1290, 1254, 1116, 1019 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.32 (d, *J* = 7.2 Hz, 3H), 1.44−1.54 (m, 1H), 1.63 (dd, *J* = 13.6, 10.1 Hz, 1H), 1.78−1.86 (m, 1H), 1.88 (ddd, *J* = 18.0, 6.4, 3.5 Hz, 1H), 2.06−2.16 (m, 2H), 2.20 (ddd, *J* = 18.0, 13.0, 6.5 Hz, 1H), 2.36 (ddd, *J* = 18.4,

dx.doi.org/10.1021/jo3014484 | J. Org. Chem. XXXX, XXX, XXX−XXX

11.0, 6.4 Hz, 1H), 2.42 (dd, J = 13.6, 9.9 Hz, 1H), 2.61 (ddd, J = 18.4, 6.6, 3.6 Hz, 1H), 2.70−2.79 (m, 1H), 2.92 (ddt, J = 17.6, 8.4, 2.8 Hz, 1H), 3.05 (ddt, J = 17.6, 5.0, 2.6 Hz, 1H), 3.76 (dd, J = 10.1, 5.8 Hz, 1H), 4.56−4.62 (m, 1H), 4.94 (ddd, J = 8.4, 5.0, 3.0 Hz, 1H), 5.61 (t, J = 2.6 Hz, 1H), 6.19 (t, J = 2.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.8 (CH_3), 24.5 (CH_2), 27.3 (CH_2), 28.6 (CH_2), 29.8 (CH_2), 33.6 (CH_2), 35.2 (CH), 35.4 (CH_2), 59.0 (CH), 65.5 (CH), 78.2 (CH), 81.1 (C), 121.8 (CH_2), 134.0 (C), 168.7 (CO), 169.7 (CO), 177.5 (CO); HRMS (ESI) calcd for [$C_{17}H_{21}NO_5$ + Na^+]: 342.1312; found: 342.1316. Compound **17b**: white solid; mp 209−211 °C (MeOH); $[\alpha]^{20}_D$ −72.4 (c 0.5, $CHCl_3$); IR (film) ν_{max} 2917, 2847, 1765, 1641, 1461, 1443, 1413, 1289, 1167, 1130, 1066 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.32 (d, J = 7.1 Hz, 3H), 1.42−1.52 (m, 1H), 1.63 (dd, J = 13.5, 10.7 Hz, 1H), 1.67−1.76 (m, 1H), 1.86−1.94 (m, 1H), 2.00 (ddt, J = 12.8, 8.3, 1.6 Hz, 1H), 2.04−2.10 (m, 1H), 2.31−2.42 (m, 2H), 2.45 (dd, J = 13.5, 9.8 Hz, 1H), 2.60 (ddt, J = 17.6, 6.4, 3.0 Hz, 1H), 2.64−2.70 (m, 1H), 2.71−2.75 (m, 1H), 3.06 (ddt, J = 17.6, 8.2, 2.6 Hz, 1H), 3.86 (dd, J = 11.0, 5.2 Hz, 1H), 4.30 (td, J = 8.1, 2.5 Hz, 1H), 5.24 (ddd, J = 8.2, 6.4, 2.5 Hz, 1H), 5.67 (t, J = 2.6 Hz, 1H), 6.26 (t, J = 3.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.7 (CH_3), 20.9 (CH_2), 27.0 (CH_2), 28.8 (CH_2), 30.0 (CH_2), 34.1 (CH_2), 35.1 (CH_2), 35.2 (CH), 60.0 (CH), 64.3 (CH), 75.2 (CH), 81.1 (C), 123.0 (CH_2), 133.6 (C), 167.5 (CO), 170.0 (CO), 177.6 (CO); HRMS (ESI) calcd for [$C_{17}H_{21}NO_5$ + Na^+] 342.1312, found 342.1315.

(−)-Sessilifoliamide J (1). A suspension of the diastereomer **17a** (6 mg, 0.02 mmol) and 10% Pd/C (5 mg) in EtOH (1 mL) was stirred under H_2 (1 atm) for 6 h. The mixture was filtered through a short pad of Celite that was washed with EtOH (2 mL). The filtrates were concentrated under reduced pressure to provide 6 mg (yield 99%) of sessilifoliamide J (**1**) as a white solid: mp 164−166 °C (MeOH) [lit.[13] mp 156−159 °C (MeOH); lit.[14] mp 164−166 °C (MeOH)]; $[\alpha]^{20}_D$ −72 (c 0.15, $CHCl_3$) [lit.[13] $[\alpha]^{26}_D$ −73 (c 0.13, $CHCl_3$); lit.[14] $[\alpha]^{20}_D$ −71 (c 0.15, $CHCl_3$)]; IR (film) ν_{max} 2964, 1773, 1637, 1450, 1407, 1384, 1263, 1096, 1018 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.27 (d, J = 7.1 Hz, 3H), 1.34 (d, J = 7.2 Hz, 3H), 1.51−1.56 (m, 1H), 1.65−1.72 (m, 2H), 1.78−1.87 (m, 1H), 1.92 (ddd, J = 13.0, 6.4, 3.8 Hz, 1H), 2.07−2.13 (m, 1H), 2.13−2.19 (m, 1H), 2.26 (ddd, J = 13.0, 11.0, 6.4 Hz, 1H), 2.35 (ddd, J = 12.7, 8.6, 5.9 Hz, 1H), 2.41 (ddd, J = 18.3, 11.0, 6.4 Hz, 1H), 2.45 (dd, J = 13.6, 10.0 Hz, 1H), 2.63−2.69 (m, 1H), 2.70 (ddd, J = 18.3, 6.4, 3.9 Hz, 1H), 2.74−2.80 (m, 1H), 3.80 (dd, J = 10.3, 5.9 Hz, 1H), 4.60 (td, J = 7.7, 4.1 Hz, 1H), 4.86 (ddd, J = 10.2, 5.5, 4.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.9 (CH_3), 16.9 (CH_3), 24.3 (CH_2), 27.3 (CH_2), 28.7 (CH_2), 32.4 (CH_2), 33.7 (CH_2), 35.2 (CH), 35.4 (CH_2), 35.5 (CH), 57.7 (CH), 65.3 (CH), 78.5 (CH), 81.2 (C), 168.4 (CO), 177.6 (CO), 178.7 (CO); HRMS (ESI) calcd for [$C_{17}H_{23}NO_5$ + Na^+] 344.1474, found 344.1477.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra of all new compounds; NOESY spectra of compound **14**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: pqhuang@xmu.edu.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are grateful to the National Basic Research Program (973 Program) of China (Grant No. 2010CB833200), the NSF of China (20832005, 21072160), and the Fundamental Research Funds for the Central Universities of China (Grant No. 201112G001) for financial support. We are grateful to Prof. Dr. L.-F. Xie for valuable discussions.

■ REFERENCES

(1) For a comprehensive review, see: Greger, H. *Planta Med.* **2006**, *72*, 99−113.

(2) (a) Sakata, K.; Aoki, K.; Chang, C.-F.; Sakurai, A.; Tamura, S.; Murakoshi, S. *Agric. Biol. Chem.* **1978**, *42*, 457−463. (b) Ye, Y.; Qin, G.-W.; Xu, R.-S. *Phytochemistry* **1994**, *37*, 1205−1208.

(3) (a) Frankowski, K. J.; Setola, V.; Evans, J. M.; Neuenswander, B.; Roth, B. L.; Aubé, J. *Proc. Nat. Acad. Sci. U.S.A.* **2011**, *108*, 6727−6732. (b) Xu, Y.-T.; Hon, P.-M.; Jiang, R.-W.; Cheng, L.; Li, S.-H.; Chan, Y.-P.; Xu, H.-X.; Shaw, P.-C.; But, P. P.-H. *J. Ethnopharmacol.* **2006**, *108*, 46−53.

(4) For reviews on the synthetic studies, see: (a) Pilli, R. A.; Rosso, G. B.; De Oliveira, M. d. C. F. *Nat. Prod. Rep.* **2000**, *17*, 117−127. (b) Alibés, R.; Figueredo, M. *Eur. J. Org. Chem.* **2009**, 2421−2435. (c) Pilli, R. A.; Rosso, G. B.; De Oliveira, M. d. C. F. *Nat. Prod. Rep.* **2010**, *27*, 1908−1937.

(5) For recent syntheses of (−)-stemoamide, see: (a) Jacobi, P. A.; Lee, K. *J. Am. Chem. Soc.* **2000**, *122*, 4295−4303. (b) Gurjar, M. K.; Reddy, D. S. *Tetrahedron Lett.* **2002**, *43*, 295−298. (c) Sibi, M. P.; Subramanian, T. *Synlett* **2004**, 1211−1214. (d) Olivo, H. F.; Tovar-Miranda, R.; Barragán, E. *J. Org. Chem.* **2006**, *71*, 3287−3290. (e) Torssell, S.; Wanngren, E.; Somfai, P. *J. Org. Chem.* **2007**, *72*, 4246−4249. For a racemic synthesis, see: (f) Wang, Y.; Zhu, L.-L.; Zhang, Y.-Y.; Hong, R. *Angew. Chem., Int. Ed.* **2011**, *50*, 2787−2790.

(6) For the synthesis of (+)-croomine, see: (a) Williams, D. R.; Brown, D. L.; Benbow, J. W. *J. Am. Chem. Soc.* **1989**, *111*, 1923−1925. (b) Martin, S. F.; Barr, K. J. *J. Am. Chem. Soc.* **1996**, *118*, 3299−3300. (c) Martin, S. F.; Barr, K. J.; Smith, D. W.; Bur, S. K. *J. Am. Chem. Soc.* **1999**, *121*, 6990−6997.

(7) For the synthesis of (−)-stemonine, see: Williams, D. R.; Shamim, K.; Reddy, J. P.; Amato, G. S.; Shaw, S. M. *Org. Lett.* **2003**, *5*, 3361−3364.

(8) For the synthesis of (−)-tuberostemonine, see: (a) Wipf, P.; Rector, S. R.; Takahashi, H. *J. Am. Chem. Soc.* **2002**, *124*, 14848−14849. (b) Wipf, P.; Spencer, S. R. *J. Am. Chem. Soc.* **2005**, *127*, 225−235.

(9) For synthesis of (−)-stemospironine, see: Williams, D. R.; Fromhold, M. G.; Earley, J. D. *Org. Lett.* **2001**, *3*, 2721−2724.

(10) For a recent synthesis of (−)-stenine, see: Chen, J. B.; Chen, J. C.; Xie, Y.; Zhang, H. B. *Angew. Chem., Int. Ed.* **2012**, *51*, 1024−1027.

(11) For synthesis of other *Stemona* alkaloids, see: (a) Taniguchi, T.; Tanabe, G.; Muraoka, O.; Ishibashi, H. *Org. Lett.* **2008**, *10*, 197−199. (b) Zhao, Y.-M.; Gu, P.-M.; Tu, Y.-Q.; Fan, C.-A.; Zhang, Q.-W. *Org. Lett.* **2008**, *10*, 1763−1766. (c) Hoye, A. T.; Wipf, P. *Org. Lett.* **2011**, *13*, 2634−2637. (d) Chen, Z.-H.; Tu, Y.-Q.; Zhang, S.-Y.; Zhang, F.-M. *Org. Lett.* **2011**, *13*, 724−727. (e) Chen, Z.-H.; Zhang, Y.-Q.; Chen, Z.-M.; Tu, Y.-Q.; Zhang, F.-M. *Chem. Commun.* **2011**, *47*, 1836−1838. (f) Chen, Z.-H.; Tu, Y.-Q.; Zhang, S.-Y.; Zhang, F.-M. *Sci. Sin. Chim.* **2011**, *41*, 474−478. (g) Chen, Z.-H.; Chen, Z.-M.; Zhang, Y.-Q.; Tu, Y.-Q.; Zhang, F.-M. *J. Org. Chem.* **2011**, *76*, 10173−10186.

(12) For a recent model studies towards the total synthesis other *Stemona* alkaloids, see: Swamy, N. K.; Pyne, S. G. *Heterocycles* **2012**, *84*, 473−492.

(13) Hitotsuyanagi, Y.; Takeda, E.; Fukaya, H.; Takeya, K. *Tetrahedron Lett.* **2008**, *49*, 7376−7379.

(14) Tuo, S.-C.; Ye, J.-L.; Wang, A.-E; Huang, S.-Y.; Huang, P.-Q. *Org. Lett.* **2011**, *13*, 5270−5273.

(15) For recent examples, see: (a) Lan, H.-Q.; Ye, J.-L.; Wang, A.-E; Huang, P.-Q. *Chem.—Eur. J.* **2011**, *17*, 958−968. (b) Lin, G.-J; Zheng, X.; Huang, P.-Q. *Chem. Commun.* **2011**, *47*, 1545−1547. (c) Chen, G.-Y.; Ye, J.-L.; Huang, H.-Y.; Ruan, Y.-P.; Wang, A.-E; Huang, P.-Q. *Chem. Asian J.* **2012**, *7*, 504−518.

(16) For a review on the synthesis of lactones, see: Paryzek, Z.; Skiera, I. *Org. Prep. Proceed. Intern.* **2007**, *39*, 203−296.

(17) For reviews/accounts on vinylogous Mannich reactions, see: (a) Casiraghi, G.; Zanardi, F.; Appendino, G.; Rassu, G. *Chem. Rev.* **2000**, *100*, 1929−1972. (b) Bur, S. K.; Martin, S. F. *Tetrahedron* **2001**, *57*, 3221−3242. (c) Martin, S. F. *Acc. Chem. Res.* **2002**, *35*, 895−904.

(18) (a) Hanessian, S.; McNaughton-Smith, G. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 1567−1572. (b) Rassu, G.; Carta, P.; Pinna, L.; Battistini, L.; Zanardi, F.; Acquotti, D.; Casiraghi, G. *Eur. J. Org. Chem.* **1999**, 1395−1400.
(19) Martin, S. F.; Bur, S. K. *Tetrahedron* **1999**, *55*, 8905−8914.
(20) (a) Martin, S. F.; Corbett, J. W. *Synthesis* **1992**, 55−56. (b) Morimoto, Y.; Nishida, K.; Hayashi, Y.; Shirahama, H. *Tetrahedron Lett.* **1993**, *34*, 5773−5776. (c) Bur, S. K.; Martin, S. F. *Org. Lett.* **2000**, *2*, 3445−3447.
(21) For a recent book on application of SmI_2 in organic synthesis, see: (a) Procter, D. J.; Flowers, R. A.; Skrydstrup, T. *Organic Synthesis Using Samarium Diiodide: A Practical Guide*; Royal Society of Chemistry: Cambridge, 2010. For reviews on SmI_2, see: (b) Kagan, H. B. *Tetrahedron* **2003**, *59*, 10351−10372. (c) Gopalaiah, K.; Kagan, H. B. *New J. Chem.* **2008**, *32*, 607−637.
(22) (a) Kawatsura, M.; Dekura, F.; Shirahama, H.; Matsuda, F. *Synlett* **1996**, 373−376. (b) Fukuzawa, S.-i.; Seki, K.; Tatsuzawa, M.; Mutoh, K. *J. Am. Chem. Soc.* **1997**, *119*, 1482−1483. (c) Matsuda, F.; Kawatsura, M.; Dekura, F.; Shirahama, H. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2371−2375. (d) Xu, M.-H.; Wang, W.; Xia, L.-J.; Lin, G.-Q. *J. Org. Chem.* **2001**, *66*, 3953−3962. (e) Fukuzawa, S.-i.; Miura, M.; Saitoh, T. *J. Org. Chem.* **2003**, *68*, 2042−2044. (f) Kerrigan, N. J.; Hutchison, P. C.; Heightman, T. D.; Procter, D. J. *Chem. Comm* **2003**, 1042−1043.
(23) Rauter, A. P.; Figueiredo, J.; Ismael, M.; Canda, T.; Font, J.; Figueredo, M. *Tetrahedron: Asymmetry* **2001**, *12*, 1131−1146.
(24) Sessilifoliamide J and 9-*epi*-sessilifoliamide J were numbered according to ref 13, which is different from the numbering for compounds **6**−**17**. As a consequence, C8 and C8a for the latter compounds correspond to C9 and C9a in sessilifoliamide J and 9-*epi*-sessilifoliamide J.
(25) Corey, E. J.; Zheng, G. Z. *Tetrahedron Lett.* **1997**, *38*, 2045−2048.

dx.doi.org/10.1021/jo3014484 | *J. Org. Chem.* XXXX, XXX, XXX−XXX