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SPECIAL FEATURE: ARTICLE

Formal syntheses of (−)-isoretronecanol, (+)-laburnine, and a concise enantioselective synthesis of (+)-turneforcidine

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Abstract

The synthesis of functionalized pyroglutamates **15** and **16** could be achieved by the application of recently developed diastereodivergent asymmetric Michael addition reaction of iminoglycinate **7** to ethyl γ-silyloxycrotonate with >98:<2 diastereoselectivity followed by hydrolysis and lactamization. Formal syntheses of (−)-isoretronecanol and (+)-laburnine as well as a concise enantioselective synthesis of (+)-turneforcidine could be achieved from functionalized pyroglutamates **15** or **16**.

Introduction

Pyrrolizidine alkaloids are azabicyclo [3.3.0]octane **1** based natural products [1, 2], which exist widely in various plant families and insects [3]. They have been shown to possess biological activities such as tumor inhibitory activities [3–6]. Some of them could be considered as antifeedants, which can be used as insecticides and anthelmintics [7]. 1-Hydroxymethyl substituted pyrrolizidines such as (−)-isoretronecanol **2** and (+)-laburnine **3** belong to a subclass of pyrrolizidine alkaloids [8]. 1-Hydroxymethyl-7-hydroxy substituted pyrrolizidines, such as (+)-turneforcidine **4**, (−)-hastanecine **5**, and (−)-platynecine **6** belong to another subclass, which are even more often seen in nature as synthetic targets [8] (Fig. 1). Asymmetric syntheses of these pyrrolizidines have attracted attention for several decades, and most reported synthetic strategies are either employing chiral auxiliary approaches [8–14], enantioselective catalysis [15, 16], or diastereoselective synthesis using accessible chiral building block that derived from L-proline [17], (*R*)- or (*S*)-malic acid [18, 19], and carbohydrates [8, 20].

Recently, we reported the syntheses of (+)-α-allokainic acid and (−)-2-*epi*-α-allokainic acid employing ketopinic amide as chiral auxiliary (Scheme 1) [21]. Asymmetric Michael reaction of iminoglycinate **7** to α,β-unsaturated esters has been developed with excellent diastereoselectivity. Moreover, a reversal of diastereoselectivity for Michael reaction at C2 of Michael adducts **8** could be controlled by the replacement of metal ions. The synthesis of functionalized pyroglutamates could be attained via the hydrolysis of Michael adducts followed by lactam formation with the recovery of chiral auxiliary. Functionalized pyroglutamates **9** are good precursors for the syntheses of alkaloid, such as pyrrolizidine **1** and indolizidine **10** natural products, which contain pyrrolidine ring (Fig. 2). Here, we report concise enantioselective synthesis of (+)-turneforcidine **4** as well as formal synthesis of (−)-isoretronecanol **2** and (+)-laburnine **3**.

Results and discussion

Our retrosynthetic analysis for (−)-isoretronecanol **2**, (+)-laburnine **3**, and (+)-turneforcidine **4** are outlined in Scheme 2. (−)-Isoretronecanol **2** and (+)-laburnine **3**, in principle, could be prepared from pyrrolizidines **11** and **12**, respectively, via reductions of double bond and amido group, and TBS group deprotection. Bsaed on a previous literature [22], epoxidation was favored to occur on less hinder *beta* face, and established C7 hydroxyl group with

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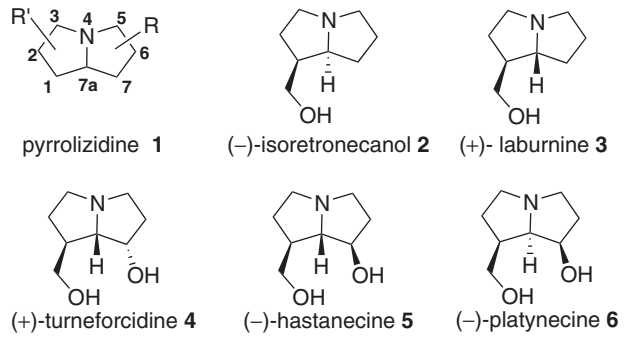


Fig. 1 1-Hydroxymethyl substituted pyrrolizidines **2-3** and 1-hydroxymethyl-7-hydroxy substituted pyrrolizidines **4-6**

correct configuration after lithium aluminum hydride (LAH) reduction. Therefore, (+)-turneforcidine **4** could be synthesized from pyrrolizidine **12** by epoxidation and followed by simultaneous epoxide opening and amide reduction with LAH. In principle, pyrrolizidines **11** and **12** could be derived from dienes **13** and **14** respectively by ruthenium-catalyzed ring-closing metathesis (RCM) [23]. The olefinic groups in dienes **13** and **14** could be obtained from lactams **15** and **16**, respectively, through allylation on amide nitrogen atom, reduction of ester group to aldehyde, and followed by a Wittig olefination. Lactams **15** and **16** could be prepared from the hydrolysis of Michael adduct that derived from a stereoselective Michael reaction of iminoglycinate **7** with γ-silyloxycrotonate **17** (Scheme 2).

The synthesis of (−)-isoretronecanol **2**, (+)-laburnine **3**, and (+)-turneforcidine **4** commenced with the preparation of pyroglutamate **15** (Scheme 3). Treatment of iminoglycinate **7** with LDA at −78 °C followed by the addition of α,β-unsaturated ester **17a** [24] gave Michael adduct **18** as single product in 91% yield. The stereochemistry of Michael adduct **18** was assigned as (2*R*,3*S*) according our previous findings [21]. Hydrolysis of Michael adduct **18** was performed with 15% citric acid to avoid the hydrolysis of ester groups and desilylation of Michael adduct [25]. Lactam **15** was obtained in 65% yield (2 steps) with a recovery of 95% ketopinic amide **19** after heating of the above hydrolysis product in methanol.

With lactam **15** in hand, we turned to synthesize the pyrrolizidine core structure. *N*-Allylation of lactam **15** with NaH and allyl iodide gave lactam **20** in 85% yield. Reduction of *tert*-butyl ester group on lactam **20** with DIBAL-H to aldehyde followed by Wittig olefination with methylenetriphenylphosphorane, prepared from methyltriphenylphosphonium bromide with fresh LHMDS, gave a 10:1 inseparable diene mixture **13** and **14** in 54% yield. The stereochemistry at C4 of dienes **13** and **14** are temporarily assigned as *S* and *R*, respectively. The formation of minor diene **14** is presumably due to an epimerization at C4 during DIBAL-H reduction and/or Wittig olefination. The stereochemistry at C4 of dienes **13** and **14** will be confirmed at a later stage. The diene mixture **13** and **14** was heated with a catalytic amount of the second-generation Grubbs catalyst [26] in dichloromethane to afford pyrrolizidines **11** and **12** in 83 and 8% yields, respectively (Scheme 4). Pyrrolizidines **11** and **12** could be separated easily by silica gel column chromatography.

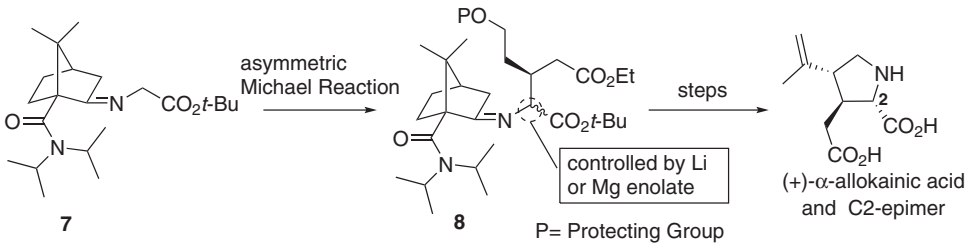
Catalytic hydrogenation (Pd/C) of pyrrolizidine **11** in EtOAc generated compound **21** in 95% yield and deprotection of the TBS group with HF gave compound **22**. Reduction of **22** to (−)-isoretronecanol **2** has been reported in previous literatures [14, 27] (Scheme 5). The spectral data of compound **22** were in agreement with the reported values [27]. The stereochemical assignments for C4 of compounds **11**–**14** are confirmed at this stage. Thus, a formal synthesis of (−)-isoretronecanol **2** was achieved in 10 synthetic steps from iminoglycinate **7**.

To establish correct stereochemistry at C7a for the syntheses of (+)-laburnine **3** and (+)-turneforcidine **4**, diastereoselective Michael addition of iminoglycinate **7** to α,β-unsaturated ester **17a** with MDA (magnesium diisopropylamide) [21] was conducted and Michael adduct **23** was obtained as sole product. The stereochemistry at C2 in **23** was assigned as *S*-configuration based on our previous study [21] and is in agreement with the required stereochemistry at C7a for (+)-laburnine **3** and (+)-turneforcidine **4**. With Michael adduct **23** in hand, one could follow the same synthetic protocol as for the synthesis of pyrrolizidine **11** (Scheme 4) to attain pyrrolizidine **12** as the major product (Scheme 6). Thus, treatment of Michael adduct **23** with 15% citric acid followed by heating in methanol gave lactam **16** in 66% yield with a recovery of **19** in 95% yield. *N*-Allylation of lactam **16** with NaH and allyl iodide gave lactam **24** in 82% yield. Reduction of *tert*-butyl ester group on lactam **24** with DIBAL-H to aldehyde followed by Wittig olefination with methylenetriphenylphosphorane gave a 15:1 inseparable diene mixture **14** and **13** in 45% yield. With this observation and the previous one (lactam **20** to diene **13**) that a minor epimerzation at C4, it would be reasonable to assign the stereochemistry at C4 of dienes **13** and **14** are *S* and *R*, respectively.

Pyrrolizidine **25** was generated by the catalytic hydrogenation of **12** with Pd/C as catalyst. Deprotection of the TBS group in **25** with HF gave compound **26**. The conversion of compound **26** to (+)-laburnine **3** has already been reported in the literature [14, 28] (Scheme 7). The spectroscopic data of compound **26** were in agreement with the reported values [28]. A formal synthesis of (+)-laburnine **3** could be achieved in 10 synthetic steps from iminoglycinate **7**.

After completed formal syntheses of two 1-hydroxymethyl substituted pyrrolizidines, we tried to synthesize (+)-turneforcidine **4**. For the synthesis of

Scheme 1 Enantioselective synthesis of (+)-α-allokainic acid and Its C2-epimer [21]



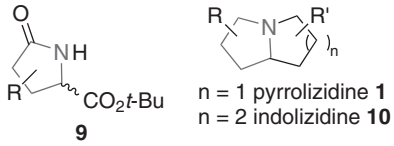


Fig. 2 Core structures of pyroglutamates, pyrrolizidines and indolizidines

(+)-turneforcidine **4**, it required the introduction of a hydroxyl group at C7 and reduction of lactam in pyrrolizidine **12**. In order to incorporate a hydroxyl group at C7 in (+)-turneforcidine **4**, epoxidation of **12** with *m*CPBA [22] was conducted first. However, it gave trace **27** with poor reactivity, and most of **12** was recovered. To solve this problem, more powerful epoxidation reagents with high reactivity toward olefins were required and dioxiranes [29] were selected for this purpose. Epoxidation of **12** using in situ prepared 3-methyl-3-trifluoromethyldioxirane [29, 30] was conducted and a single epoxide was obtained. Based on a previous report [22], epoxidation of C5, C6 double bond occurred from the concave face of of the pyrrolidine and the stereochemistry was temporarily assigned as depicted in **27**. Finally, treatment of epoxide **27** with lithium aluminium hydride (LAH) resulted in concomitant ring opening of epoxide, desilylation [31], and amide reduction afforded (+)-turneforcidine **4** in 75% yield (Scheme 7). The spectral and physical data were in accord with the reported data [32]. (+)-Turneforcidine **4** was achieved in nine synthetic steps with 12% overall yield from iminoglycinate **7**.

Conclusion

Enantioselective formal syntheses of pyrrolizidine alkaloids (−)-isoretronecanol **2**, (+)- laburnine **3**, and a total synthesis of (+)-turneforcidine **4** were accomplished. The syntheses started with Michael reaction of the enolate from iminoglycinate **7** to α,β-unsaturated ester **17a** in high diastereoselectivity as key step. Subsequent hydrolysis of the Michael adduct generated functionalized pyroglutamate, and provided a concise pathway to the corresponding pyrrolizidine alkaloids (−)-isoretronecanol **2**, (+)-laburnine **3**, and (+)-turneforcidine **4** from functionalized pyroglutamates **15** or **16**. Thus, a facile entry for the synthesis of pyrrolizidine alkaloids had been demonstrated.

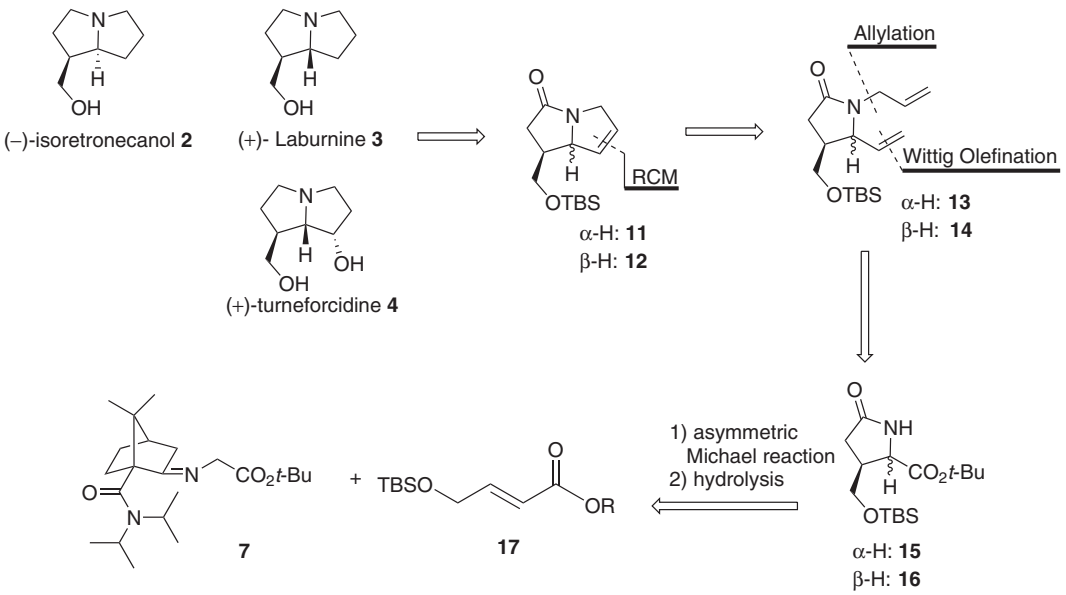
Experimental section

General information

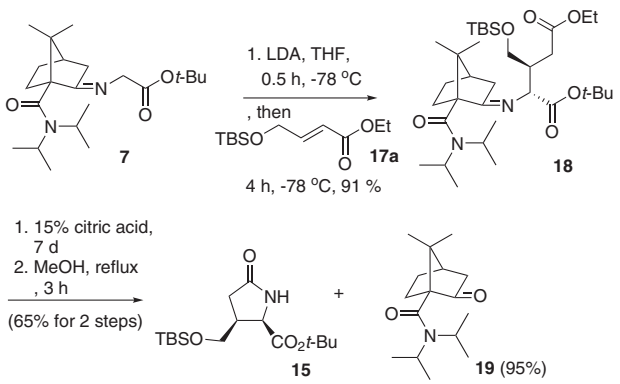
Reagents were obtained from commercial sources and used without further purification. Most reactions were performed under an argon atmosphere in anhydrous solvents, which were dried prior to use following standard procedures. Merck Art. No. 7734 and 9385 silica gels were employed for flash chromatography. Analytical TLC was conducted on DC Aluminiumoxid 150 F_{254}, neutral, and chromatograms were visualised with aq. $KMnO_4$. ^1H NMR spectra were obtained and noted at 400 MHz (Bruker DPX-400 or Varian-Unity-400). ^{13}C NMR spectra were obtained at 100 MHz. Chemical shifts are reported in values, in parts per million (ppm) relative to residual chloroform (7.26 ppm for ^1H NMR, 77.00 ppm for ^{13}C NMR) or H_2O (4.80 ppm for ^1H NMR) as an internal standard. The multiplicities of the signals are described using the following abbreviations: *s* = singlet, *d* = doublet, *t* = triplet, *q* = quartet, dd = doublet of doublets, *m* = multiplet, br = broad band. The melting point was recorded on a melting point apparatus (Buchi 512– melting point system) and is uncorrected. IR spectra were performed in a spectrophotometer Bomen MB 100 FT-IR and only noteworthy IR absorptions (cm^{-1}) are listed. Optical rotations were measured on Perkin-Elmer 241 polarimeter. Mass spectrometric analyses were performed by the Center for Advanced Instrumentation and Department of Applied Chemistry at National Chiao Tung University, Hsinchu, Taiwan.

Ethyl (*E*)-4-hydroxybut-2-enoate (28)

A solution of commercial-available monoethyl fumarate (5.00 g, 34.7 mmol) in THF (34.7 mL) was added $BH_3{\cdot}Me_2S$ (17.3 mL, 34.7 mmol, 2.00 M in THF) at –10 °C for a period of 10 min [33]. The reaction mixture was allowed to warm to room temperature and stirred for 16 h. The reaction mixture was quenched with 5 mL of 50% AcOH, concentrated, and the residual slurry was treated



Scheme 2 Retrosynthetic analysis for **2**, **3**, and **4**



Scheme 3 Synthesis of lactam **15** from iminoglycinate **7**

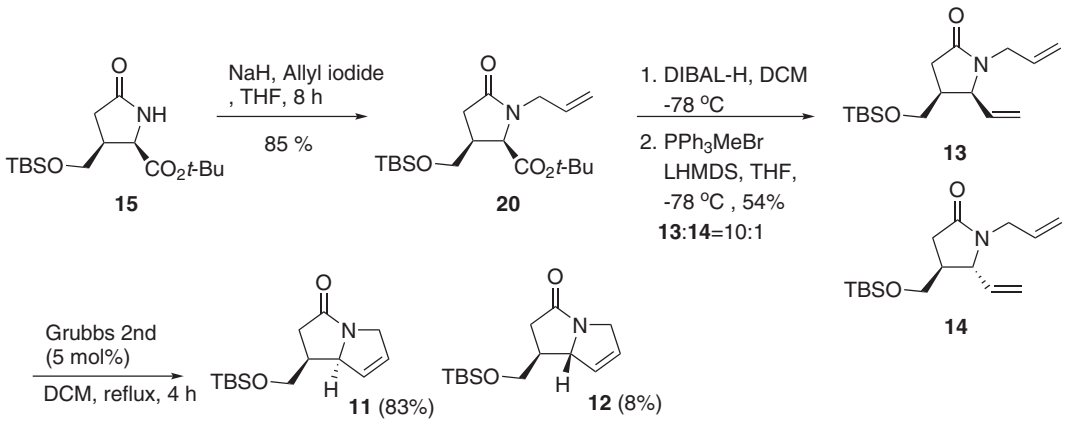
with saturated aqueous $NaHCO_3$ at 0 °C. The resulting mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with water, brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by flash chromatography (eluent: EtOAc/Hexanes, 1/3) to provide **28** (1.58 g, 12.1 mmol, 35%) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.92 (dt, $J = 16.0$, 3.6 Hz, 1 H), 5.98 (dt, $J = 16.0$, 2.0 Hz, 1 H), 4.21−4.10 (m, 2 H), 4.09 (q, $J = 6.8$ Hz, 2 H), 3.47 (br, 1 H), 1.19 (t, $J = 6.8$ Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.2, 147.3, 118.9, 60.6, 59.8, 13.4.

Ethyl (*E*)-4-((*tert*-butyldimethylsilyl)oxy)but-2-enoate (17a)

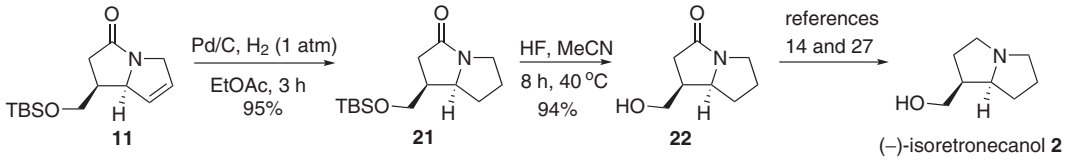
A solution of allyl alcohol **28** (2.54 g, 19.6 mmol) in CH_2Cl_2 (15 mL) was added Et_3N (3.25 mL, 23.5 mmol), and DMAP (119 mg, 0.98 mmol) at 0 °C [24]. The reaction mixture was stirred at 0 °C for 5 min, and the solution of TBSCl (2.56 g, 19.6 mmol) in THF (5 mL) was added slowly. The reaction mixture was allowed to warm to room temperature and stirred for 5 h. The reaction mixture was quenched by sat. $NaHCO_3$ aq and extracted with EtOAc (3 × 10 mL). The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by flash chromatography (eluent: EtOAc/Hexanes, 1/6) to provide **17a** (4.53 g, 18.6 mmol, 95%) as colorless oil. $R_f = 0.52$ (EtOAc/Hexanes, 1/4); IR (neat) 2979, 2936, 2863, 2290, 1732, 1682, 1515, 1456, 1422, 1369, 1301, 1249, 1156, 1095, 1034 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.95 (dt, $J = 15.4$, 3.4 Hz, 1 H), 6.05 (dt, $J = 15.4$, 2.3 Hz, 1 H), 4.29 (dd, $J = 3.3$, 2.3 Hz, 2 H), 4.15 (q, $J = 7.1$ Hz, 2 H), 1.24 (t, $J = 7.1$ Hz, 3 H), 0.88 (s, 9 H), 0.04 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.5, 147.2, 119.5, 62.0, 60.1, 25.7 (3 C), 18.2, 14.2, −5.6 (2 C); HRMS (HRFD) m/z: $[M]^+$ Calcd for $C_{12}H_{24}O_3Si$ 244.1495; Found 244.1493.

1-*tert*-Butyl ethyl (2*R*,3*S*)-*N*-2-(((1*R*,4*R*)-1-(*N*,*N*-diisopropylaminocarbonyl)-7,7-dimethylbicyclo [2.2.1]heptan-2-ylidene)amino)-3-((*tert*-butyldimethylsilyl)oxy)-methyl) glutamate (18)

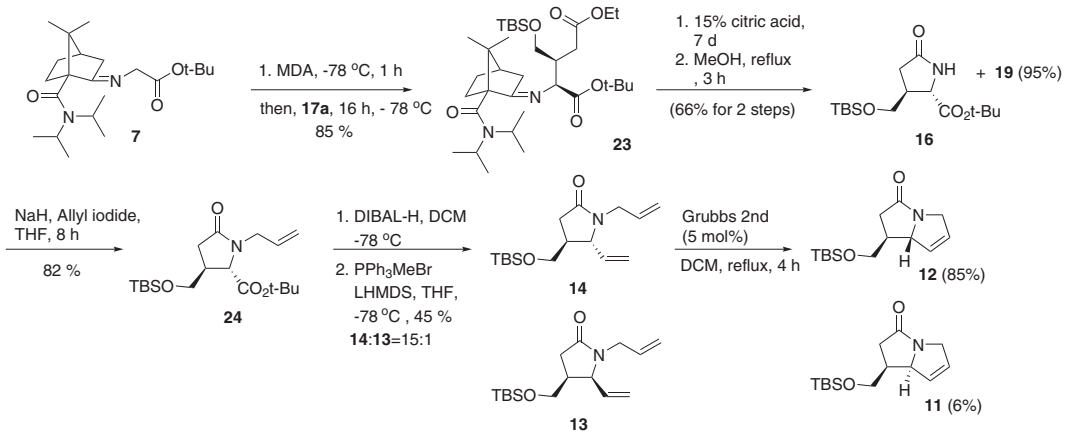
A solution of LDA in THF was prepared under argon with diisopropylamine (0.55 mL, 3.96 mmol), THF (4.2 mL), and *n*-BuLi solution (2.30 M solution in hexane, 1.61 mL, 3.70 mmol) at 0 °C. After stirring for 30 min, the solution was cooled to −78 °C with a dry ice-acetone



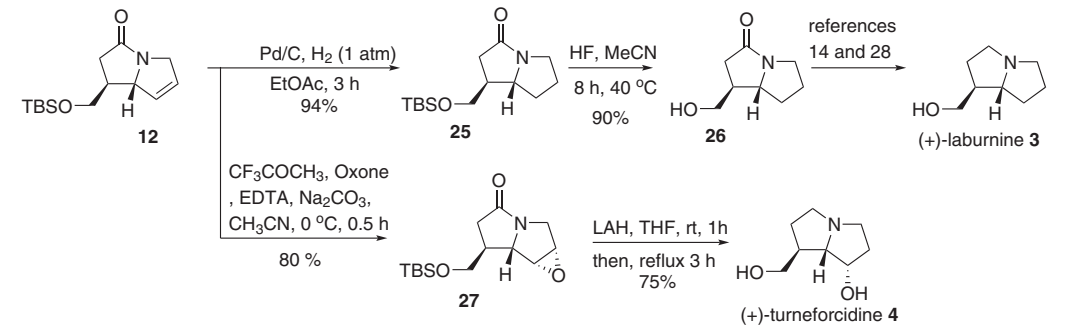
Scheme 4 Synthesis of pyrrolizidine **11** and **12**



Scheme 5 Synthesis of (−)-isoretronecanol **2**



Scheme 6 Synthesis of pyrrolizidine **12** as major product



Scheme 7 Syntheses of (+)-laburnine **3** and (+)-turneforcidine **4**

bath and a solution of iminoglycinate 7 (1.00 g, 2.64 mmol) in THF (1.8 mL) was added over 20 min. The mixture was stirred for 30 min, then a solution of **17a** (0.77 g, 3.17 mmol) in THF (0.8 mL) was added slowly. The mixture was stirred for 4 h at −78 °C, then a solution of 2% $H_2C_2O_4$(aq) (10 mL) was added. The reaction mixture was warmed to 0 °C then was neutralized with additional 2% $H_2C_2O_4$(aq) to pH = 6~7. The aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic phases were washed with brine (20 mL), dried over anhydrous Na_2SO_4, and evaporated *in vacuo*. The residue was purified by flash chromatography (eluent: EtOAc/Hexanes, 1/8 + 1% Et_3N) to provide **18** (1.50 g, 2.40 mmol, 91%) as colorless liquid. $R_f = 0.50$ (EtOAc/Hexanes, 1/6); $[\alpha]_D^{22}$–2.4 (*c* 1.0, CH_2Cl_2); IR (neat) 2959, 2931, 2859, 1730, 1675, 1631, 1367, 1335, 1253, 1162, 836, 777 cm^{-1}; ^1H

NMR (400 MHz, $CDCl_3$): δ 4.25−4.16 (m, 1 H), 4.07 (q, $J = 7.2$ Hz, 2 H), 3.97 (d, $J = 8.9$ Hz, 1 H), 3.70−3.56 (m, 1 H), 3.45 (dd, $J = 9.9$, 3.6 Hz, 1 H), 3.28 (septet, $J = 6.8$ Hz, 1 H), 2.72-2.52 (m, 2 H), 2.51−2.41 (m, 1 H), 2.35 (dd, $J = 16.0$, 3.7 Hz, 1 H), 2.22−2.07 (m, 1 H), 2.01−1.83 (m, 3 H), 1.77−1.68 (m, 1 H), 1.45−1.35 (m, 2 H), 1.37 (s, 9 H), 1.33 (d, $J = 6.6$ Hz, 3 H), 1.22 (t, $J = 7.1$ Hz, 3 H), 1.19 −1.14 (m, 1 H), 1.17 (d, $J = 6.6$ Hz, 3 H), 1.09 (s, 3 H), 1.04 (d, $J = 6.6$ Hz, 3 H), 0.95 (dd, $J = 10.3$, 6.6 Hz, 2 H), 0.89−0.81 (m, 2 H), 0.86 (s, 9 H), 0.00 (s, 3 H), −0.01(s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.3, 172.6, 170.0, 169.7, 81.1, 66.1, 65.4, 60.8, 60.2, 51.8, 48.1, 46.0, 43.9, 39.8, 36.2, 32.0, 29.2, 27.8 (3C), 27.2, 25.9 (3C), 23.1, 21.8, 20.8, 20.6, 20.5, 20.3, 18.2, 14.2, −5.6 (2C); HRMS (HRFD) m/z: $[M]^+$ Calcd for $C_{34}H_{62}N_2O_6Si$ 622.4372; Found 622.4366.

1-*tert*-Butyl ethyl (2 *S*,3 *S*)-*N*-2-(((1 *R*,4 *R*)-1-(*N*,*N*-diisopropylaminocarbonyl)-7,7-dimethylbicyclo [2.2.1]heptan-2-ylidene)amino)-3-((*tert*-butyldimethylsilyl)oxy)-methyl) glutamate (23)

A solution of MDA in THF was prepared under argon with diisopropylamine (0.56 mL, 3.96 mmol), THF (6.7 mL), and methylmagnesium bromide solution (1.00 M solution in THF, 3.70 mL, 3.70 mmol) at 0 °C. After stirring for 30 min, the solution was cooled to –78 °C with a dry ice-acetone bath and a solution of iminoglycinate **7** (1.00 g, 2.64 mmol) in THF (1.80 mL) was added over 20 min. The mixture was stirred for 1 h, then a solution of **17a** (0.64 g, 2.64 mmol) in THF (2.6 mL) was added slowly. The mixture was warmed to −60 °C, and stirred for an additional 18 h, then a solution of 2% $H_2C_2O_4$(aq) (10 mL) was added. The reaction mixture was warmed to 0 °C then neutralized with additional 2% $H_2C_2O_4$(aq) to *p*H = 7~8. The aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic phases were washed with brine (20 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by flash chromatography (eluent: EtOAc/Hexanes, 1/8 + 1% Et_3N) to provide **23** (1.40 g, 1.85 mmol, 85%) as pale yellow oil. $R_f = 0.52$ (EtOAc/Hexanes, 1/6); $[\alpha]_D^{22} + 5.6$ (*c* 1.0, CH_2Cl_2); IR (neat) 2959, 2931, 2886, 1735, 1678, 1630, 1367, 1335, 1254, 1157, 1100, 836, 777 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.26 (septet, $J = 6.6$ Hz, 1 H), 4.17 (d, $J = 5.0$ Hz, 1 H), 4.07 (q, $J = 7.1$ Hz, 2 H), 3.60 (dd, $J = 10.1$, 5.1 Hz, 1 H), 3.38−3.22 (m, 2 H), 2.74−2.63 (m, 1 H), 2.52 (dd, $J = 16.2$, 3.3 Hz, 1 H), 2.24 (dd, $J =$ 16.2, 9.8 Hz, 1 H), 2.14−2.05 (m, 1 H), 2.03−1.88 (m, 2 H), 1.82 (d, $J = 3.7$ Hz, 1 H), 1.73 (t, $J = 4.4$ Hz, 1 H), 1.42 (s, 9 H), 1.40 (d, $J = 6.8$ Hz, 3 H), 1.34 (d, $J = 6.8$ Hz, 3 H), 1.30−1.22 (m, 1 H), 1.20 (t, $J = 7.1$ Hz, 3 H), 1.15 (d, $J = 6.3$ Hz, 3 H), 1.13 (s, 6 H), 1.04 (d, $J = 6.9$ Hz, 3 H), 0.86 (d, $J = 1.3$ Hz, 1 H), 0.84 (s, 9 H), 0.00 (s, 3 H), −0.01(s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.4, 173.0, 170.3, 170.0, 80.7, 65.3, 63.4, 62.5, 60.1, 50.5, 48.1, 46.0, 43.9, 40.1, 35.5, 32.3, 28.6, 28.0 (3 C), 27.4, 25.8 (3 C), 21.8, 21.6, 20.9 (2 C), 20.3 (2 C), 18.1, 14.2, −5.5 (2 C); HRMS (ESI) m/z: $[M_+H]^+$ Calcd for $C_{34}H_{63}N_2O_6Si$ 623.4450; Found 623.4452.

tert-Butyl (2 *R*,3 *S*)-3-(((*tert*-butyldimethylsilyl)oxy) methyl)-5-oxopyrrolidine-2-carboxylate (15)

A solution of **18** (1.37 g, 2.20 mmol) in THF (7.4 mL) was added a solution of 15 % aqueous citric acid (4.8 mL, 2.3 mmol). The mixture was stirred at room temperature for 7 day. After evaporation of THF, the residue was dissolved in H_2O (5 mL). The aqueous phase was adjusted to pH 7 using Na_2CO_3 and extracted with dichloromethane (3 × 30 mL). The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The crude amino ester was used without purification. The crude amino ester was dissolved in MeOH (7.4 mL). The mixture was refluxed for 3 h, then MeOH was evaporated *in vacuo*. The residue was purified by flash chromatography (eluent: EtOAc/Hexanes, 1/2 to DCM/MeOH, 10/1) to provide 15 (470 mg, 1.43 mmol, 65%) as colorless liquid and recover auxiliary 19 (555 mg, 2.09 mmol, 95%). $R_f = 0.52$ (DCM/ MeOH, 20/1); $[\alpha]_D^{23}$ −3.4 (*c* 1.0, CH_2Cl_2); IR (neat) 3232, 2956, 2930, 2886, 1712, 1632, 1473, 1392, 1368, 1253, 1229, 1157, 1104, 1006, 939, 838 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.92 (br, 1 H), 4.12 (d, $J = 7.7$ Hz, 1 H), 3.71−3.62 (m, 1 H), 3.48 (t, $J = 9.0$ Hz, 1 H), 2.84−2.67 (m, 1 H), 2.36 (dd, $J =$ 16.8, 8.4 Hz, 1 H), 2.27 (dd, $J = 16.8$, 6.7 Hz, 1 H), 1.41 (s, 9 H), 0.81 (s, 9 H), 0.00 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.6, 169.4, 82.2, 62.1, 58.6, 39.8, 33.6, 27.9 (3 C), 25.6 (3 C), 18.0, −5.6 (2 C); HRMS (ESI) (m/z):

$[M + H]^+$ Calcd for $C_{16}H_{32}NO_4Si$ 330.2101; Found 330.2102.

tert-Butyl (2 *S*,3 *S*)-3-(((*tert*-butyldimethylsilyl)oxy) methyl)-5-oxopyrrolidine-2-carboxylate (16)

Starting with **23** (1.00 g, 1.60 mmol), and followed the same procedure as in the synthesis of **15** provided **16** (348 mg, 1.06 mmol, 66%) and recovered auxiliary **19** (404 mg, 1.52 mmol, 95%). $R_f = 0.31$ (EtOAc/Hexanes, 1/1); $[\alpha]_D^{25}$ −6.4 (*c* 1.0, CH_2Cl_2); IR (neat) 3233, 2955, 2930, 2886, 2858, 1738, 1708, 1369, 1252, 1158, 1110, 837, 777 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.03 (br, 1 H), 3.94 (d, $J = 5.5$ Hz, 1 H), 3.64 (dd, $J = 10.1$, 5.1 Hz, 1 H), 3.58 (dd, $J = 10.1$, 5.2 Hz, 1 H), 2.59−2.47 (m, 1 H), 2.35 (dd, $J = 17.0$, 9.1 Hz, 1 H), 2.21 (dd, $J = 16.8$, 6.6 Hz, 1 H), 1.39 (s, 9 H), 0.81 (s, 9 H), −0.01 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.3, 171.0, 82.0, 63.0, 57.5, 40.8, 32.3, 27.8 (3 C), 25.6 (3 C), 18.0, −5.6 (2 C); HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{32}NO_4Si$ 330.2101; Found 330.2095.

tert-Butyl (2 *R*,3 *S*)-1-allyl-3-(((*tert*-butyldimethylsilyl)oxy)methyl)-5-oxopyrrolidine-2-carboxylate (20)

A suspension of sodium hydride (295 mg, 7.37 mmol, 60% in mineral oil) in dry THF (60 mL) was stirred for 10 min at 0 °C, then a solution of **15** (2.21 g, 6.70 mmol) in THF (7 mL) was added and the mixture was warmed to room temperature for 30 min. After 30 min, the reaction mixture was again cooled to 0 °C, and allyl iodide (0.92 mL, 10.1 mmol) was added slowly with stirring for 8 h. Finally, the reaction mixture was quenched with sat. $NaHCO_3$(aq) solution. The organic phase was separated and the aqueous phase was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with water, brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by flash chromatography (eluent: EtOAc/Hexanes, 1/1) to provide **20** (2.10 g, 5.70 mmol, 85%) as yellow liquid. $R_f = 0.39$ (EtOAc/Hexanes, 1/2); $[\alpha]_D^{25}$−11.3 (*c* 1.0, CH_2Cl_2); IR (neat) 2955, 2930, 2858, 1735, 1707, 1472, 1409, 1368, 1252, 1156, 1110, 1006, 837, 777 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.68−5.51 (m, 1 H), 5.14−4.97 (m, 2 H), 4.13 (dd, $J = 15.2$, 5.5 Hz, 1 H), 3.92 (d, $J = 8.3$ Hz, 1 H), 3.62 (dd, $J = 10.1$, 6.8 Hz, 1 H), 3.47−3.40 (m, 1 H), 3.36 (dd, $J = 15.1$, 7.4 Hz, 1 H), 2.68−2.55 (m, 1 H), 2.31 (dd, $J = 16.5$, 8.4 Hz, 1 H), 2.20 (dd, $J = 16.5$, 10.6 Hz, 1 H), 1.34 (s, 9 H), 0.76 (s, 9 H), −0.08 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.2, 169.0, 131.9, 118.4, 82.0, 62.5, 61.8, 44.3, 38.1, 33.5, 27.7 (3 C), 25.5 (3 C), 17.9, −5.6, −5.7; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{36}NO_4Si$ 370.2414; Found 370.2417.

tert-Butyl (2 *S*,3 *S*)-1-allyl-3-(((*tert*-butyldimethylsilyl) oxy)methyl)-5-oxopyrrolidine-2-carboxylate (24)

Starting with **16** (400 mg, 1.21 mmol), and followed the same procedure as in the synthesis of **20** provided **24** (367 mg, 0.99 mmol, 82%). *R*f = 0.36 (EtOAc/Hexanes, 1/2); $[\alpha]_D^{25}$ + 29.8 (*c* 1.0, CH_2Cl_2); IR (neat) 2955, 2931, 2858, 1737, 1704, 1410, 1369, 1253, 1228, 1156, 1109, 990, 837 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.70−5.56 (m, 1 H), 5.13−5.05 (m, 2 H), 4.28 (dd, $J = 15.2$, 5.1 Hz, 1 H), 3.89 (d, $J = 3.2$ Hz, 1 H), 3.56 (dd, $J = 10.0$, 5.2 Hz, 1 H), 3.53 −3.41 (m, 2 H), 2.53 (dd, $J = 16.9$, 9.3 Hz, 1 H), 2.42−2.32 (m, 1 H), 2.15 (dd, $J = 16.9$, 3.6 Hz, 1 H), 1.41 (s, 9 H), 0.83 (s, 9 H), −0.01 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.1, 170.9, 132.0, 118.6, 82.0, 63.9, 61.8, 44.3, 38.3, 32.5, 27.9 (3 C), 25.7 (3 C), 18.1, −5.5, −5.6; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{36}NO_4Si$ 370.2414; Found 370.2415.

(4*S*,5 *S*)-1-Allyl-4-(((*tert*-butyldimethylsilyl)oxy) methyl)-5-vinylpyrrolidin-2-one (13) and (4 *S*,5 *R*)-1-allyl-4-(((*tert*-butyldimethylsilyl)oxy)methyl)-5-vinylpyrrolidin-2-one (14)

To a solution of **20** (0.50 g, 1.35 mmol) in DCM (4.5 mL) was added DIBAL-H (3.38 mL, 3.38 mmol, 1.00 M solution in toluene) at −78 °C under an argon atmosphere. After 90 min, the reaction mixture was quenched with sat. potassium sodium tartrate (aq) and warmed to room temperature. The reaction mixture was stirred vigorously for 1 h, and two phases were separated. The aqueous layer was extracted with EtOAc (3 × 15 mL). The combined organic phases were dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude aldehyde was used without purification. To a 25 mL round-bottom flask charged with methyltriphenylphosphonium bromide (675 mg, 1.89 mmol) and THF (3.4 mL) at room temperature was slowly added lithium bis(trimethylsilyl)amide (1.66 mL, 1.76 mmol, 1.06 *N* in toluene). The mixture was stirred for 0.5 h at room temperature, then was added to a solution of crude aldehyde in THF (3.4 mL) at −78 °C in a 25 mL round-bottom flask. The reaction mixture was stirred for 1 h at –78 °C, and was quenched by the addition of saturated aqueous sodium bicarbonate solution (15.0 mL) followed by the extraction with ethyl acetate (3 × 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (eluent: EtOAc/Hexanes, 1/1) to give an inseparable mixture of **13** and **14** (215 mg, 0.73 mmol, 54%; ratio 10:1). (The ratio was determined by chemical shifts at 3.32 and 3.26 ppm in ^1H NMR spectrum) **Diene 13:** $R_f = 0.27$ (EtOAc/Hexanes, 1/2); IR (neat) 2954, 2928, 2857, 1699, 1643, 1471, 1410, 1251, 1116, 1085, 991, 923, 838, 776 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.73−5.56

(m, 2 H), 5.28−5.03 (m, 4 H), 4.31 (dd, $J = 15.4$, 4.5 Hz, 1 H), 4.07 (t, $J = 8.0$ Hz, 1 H), 3.58−3.51 (m, 2 H), 3.26 (ddd, $J = 15.5$, 7.4, 1.0 Hz, 1 H), 2.64−2.53 (m, 1 H), 2.35 (dd, $J =$ 16.5, 8.5 Hz, 1 H), 2.19 (ddd, $J = 16.6$, 10.5, 0.5 Hz, 1 H), 0.83 (s, 9 H), 0.00 (s, 3 H), −0.01 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.7, 133.1, 132.4, 119.0, 117.5, 62.2, 62.2, 42.9, 39.0, 32.8, 25.7 (3 C), 18.0, −5.6 (2 C);

Diene 14

$R_f = 0.27$ (EtOAc/Hexanes, 1/2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.73−5.56 (m, 2 H), 5.28−5.03 (m, 4 H), 4.23 (dd, $J = 15.4$, 4.5 Hz, 1 H), 4.07 (t, $J = 8.0$ Hz, 1 H), 3.84 (dd, $J = 8.6$, 5.0 Hz, 1 H), 3.84−3.80 (m, 1 H), 3.32 (dd, $J = 15.5$, 7.4, 1 H), 2.64−2.53 (m, 1 H), 2.44 (dd, $J =$ 16.5, 8.5 Hz, 1 H), 2.19 (ddd, $J = 16.6$, 10.5, 0.5 Hz, 1 H), 0.83 (s, 9 H), 0.00 (s, 3 H), −0.01 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.8, 137.2, 132.2, 118.4, 117.7, 62.8, 62.2, 40.5, 39.0, 32.6, 25.7 (3 C), 18.0, −5.6 (2 C); HRMS (ESI) for a mixture of **13** and **14**, m/z: $[M + H]^+$ Calcd for $C_{16}H_{30}NO_2Si$ 296.2046; Found 296.2039.

(1 *S*,7a*S*)-1-(((*tert*-Butyldimethylsilyl)oxy)methyl)-1,2,5,7a-tetrahydro-3*H*-pyrroli- zin-3-one (11) and (1 *S*,7a*R*)-1-(((*tert*-butyldimethylsilyl)oxy)methyl)-1,2,5,7a-tetrahydro-3H-pyrrolizin-3-one (12)

To a 100 mL round-bottom flask containing a mixture of dienes **13** and **14** (200 mg, 0.68 mmol) in DCM (68 mL) was added Grubbs 2nd generation catalyst (29.0 mg, 0.03 mmol). The reaction mixture was refluxed for 4 h, then was cooled to room temperature and concentrated *in vacuo*. The residue was purified by column chromatography (eluent: EtOAc/Hexanes, 1/1) to give **11** (150 mg, 0.56 mmol, 83%, as brown liquid) and **12** (13.0 mg, 0.05 mmol, 8%, as brown liquid). **Lactam 11**: $R_f = 0.24$ (EtOAc/Hexanes, 1/1); $[\alpha]_D^{25}$ −24.4 (*c* 1.0, CH_2Cl_2); IR (neat) 2953, 2929, 2857, 1703, 1471, 1381, 1254, 1197, 1102, 1077, 1004, 938, 837, 813 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.96−5.87 (m, 1 H), 5.85−5.78 (m, 1 H), 4.80−4.72 (m, 1 H), 4.39−4.26 (m, 1 H), 3.68−3.56 (m, 1 H), 3.43 (dd, $J = 10.2$, 7.7 Hz, 1 H), 3.30 (dd, $J = 10.2$, 6.0 Hz, 1 H), 2.78 (dd, $J = 16.4$, 7.8 Hz, 1 H), 2.67 (quintet, $J = 7.1$, 1 H), 2.11 (d, $J = 16.4$ Hz, 1 H), 0.81 (s, 9 H), −0.04 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.7, 128.2, 128.0, 69.5, 62.4, 49.3, 41.2, 37.3, 25.7 (3 C), 18.1, −5.6 (2 C); HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{26}NO_2Si$ 268.1733; Found 268.1726.

Lactam 12

$R_f = 0.29$ (EtOAc/Hexanes, 1/1); $[\alpha]_D^{22} + 1.2$ (*c* 1.0, CH_2Cl_2); IR (neat) 2954, 2929, 2857, 1706, 1417, 1387, 1351, 1253, 1113, 1078 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.98−5.86 (m, 1 H), 5.85−5.76 (m, 1 H), 4.47−4.29 (m, 2 H), 3.76 (dd, $J = 10.2$, 4.4 Hz, 1 H), 3.66−3.55 (m, 2 H), 2.49 (dd, $J =$ 17.8, 11.6 Hz, 1 H), 2.43−2.30 (m, 1 H), 2.30−2.20 (dd, $J =$ 14.8, 7.6 Hz, 1 H), 0.85 (s, 9 H), 0.02 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.0, 130.6, 127.8, 71.0, 64.0, 49.7, 46.6, 36.2, 25.7 (3 C), 18.1, −5.6 (2 C); HRMS (HRFD) m/z: $[M]^+$ Calcd for $C_{14}H_{25}NO_2Si$ 267.1655; Found 267.1649.

(1 *S*,7a*S*)-1-(((*tert*-Butyldimethylsilyl)oxy)methyl) hexahydro-3*H*-pyrrolizin-3-one (21)

To a two-necked round-bottom flask containing a suspension of 5% Pd/C (12.0 mg) in EtOAc (1.3 mL) was added **11** (62.0 mg, 0.23 mmol in EtOAc (1.0 mL). The mixture was stirred vigorously for 3 h under H_2 atmosphere (1 atm), then was filtered through a short pad of Celite. The filtrate was concentrated *in vacuo* to afford **21** (59.0 mg, 0.22 mmol, 95%) as colorless oil. $R_f = 0.18$ (EtOAc/Hexanes, 1/1); $[\alpha]_D^{23}$ −26.1 (*c* 1.0, CH_2Cl_2); IR (neat) 2953, 2929, 2884, 2863, 2857, 1700, 1472, 1419, 1254, 1106, 837, 776 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.98−3.87 (m, 1 H), 3.60−3.48 (m, 2 H), 3.47−3.35 (m, 1 H), 3.06−2.96 (m, 1 H), 2.74 (dd, $J = 16.8$, 8.9 Hz, 1 H), 2.58−2.45 (m, 1 H), 2.13 (dd, $J = 16.8$, 3.2 Hz, 1 H), 2.10−2.01 (m, 1 H), 1.99−1.87 (m, 1 H), 1.78−1.68 (m, 1 H), 1.64−1.51 (m, 1 H), 0.81 (s, 9 H), −0.02 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.9, 63.8, 62.8, 40.7, 37.6, 36.2, 26.6, 25.6 (3 C), 25.3, 17.9, −5.7 (2 C); HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{28}NO_2Si$ 270.1889; Found 270.1895.

(1 *S*,7a*R*)-1-(((*tert*-Butyldimethylsilyl)oxy)methyl) hexahydro-*3H*-pyrrolizin-3-one (25)

Starting with **12** (50.0 mg, 0.19 mmol), and followed the same procedure as in the synthesis of **21** provided **25** (47.0 mg, 0.18 mmol, 94%) as colorless oil. $R_f = 0.23$ (EtOAc/Hexanes, 1/1); $[\alpha]_D^{23} + 12.1$ (*c* 1.0, CH_2Cl_2); IR (neat) 2954, 2929, 2884, 2856, 1698, 1412, 1253, 1113, 837 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.65 (dd, $J = 10.0$, 5.0 Hz, 1 H), 3.64−3.59 (m, 1 H), 3.55 (dd, $J = 10.1$, 7.3 Hz, 1 H), 3.51−3.44 (m, 1 H), 2.99 (td, $J = 9.1$, 2.9 Hz, 1 H), 2.49 (dd, $J = 16.1$, 10.8 Hz, 1 H), 2.37 (dd, $J = 16.2$, 8.4 Hz, 1 H), 2.31−2.19 (m, 1 H), 2.10−1.90 (m, 3 H), 1.44−1.29 (m, 1 H), 0.84 (s, 9 H), 0.00 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.8, 65.2, 64.3, 44.5, 41.0, 37.8, 31.6, 26.8, 25.7 (3 C), 18.1, −5.6 (2 C); HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{28}NO_2Si$ 270.1889; Found 270.1886.

(1 *S*,7a*S*)-1-(Hydroxymethyl)hexahydro-3*H*-pyrrolizin-3-one (22)

To **21** (32 mg, 0.12 mmol) and MeCN (0.6 mL) in 5 mL plastic round-bottom flask at room temperature was added

49.4% HF aqueous solution (0.02 mL, 0.36 mmol) then stirred for 8 h at 40 °C [27]. The reaction was quenched by the addition of saturated sodium bicarbonate aqueous solution (10 mL) then extracted with dichloromethane (3 × 10 mL). The combined organic layers were dried over anhydrous sodium sulfate then filtered and concentrated *in vacuo* to afford the crude material. The crude material was purified by flash chromatography (MeOH/DCM, 1/10) to provide **22** (17.0 mg, 0.11 mmol, 94%) as colorless oil. $R_f = 0.30$ (DCM/MeOH, 10/1); $[\alpha]_D^{25}$ −63.3 (*c* 1.0, EtOH); IR (neat) 3395, 2957, 2924, 2886, 2858, 1664, 1455, 1422 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.01−3.95 (m, 1 H), 3.68 (dd, $J = 10.4$, 7.6 Hz, 1 H), 3.59 (dd, $J = 10.4$, 6.4 Hz, 1 H), 3.48−3.38 (m, 1 H), 3.08−2.98 (m, 1 H), 2.79 (dd, $J = 16.8$, 8.8 Hz, 1 H), 2.63−2.55 (m, 1 H), 2.23 (dd, $J = 16.8$, 3.6 Hz, 1 H), 2.13−2.02 (m, 1 H), 2.02−1.92 (m, 1 H), 1.84−1.75 (m, 2 H), 1.62−1.54 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): 174.3, 63.8, 61.8, 44.6, 37.7, 36.1, 25.5, 25.0; HRMS (HRFD) m/z: $[M]^+$ Calcd for $C_8H_{13}NO_2$ 155.0946; Found 155.0940.

(1 *S*,7a*R*)-1-(Hydroxymethyl) hexahydro-3*H*-pyrrolizin-3-one (26)

Starting with **25** (50.0 mg, 0.19 mmol), and followed the same procedure as in the synthesis of **22** provided **26** (26.0 mg, 0.18 mmol, 90%) as colorless oil [28]. $R_f = 0.23$ (DCM/MeOH = 10/1); $[\alpha]_D^{25}$ −15.0 (*c* 0.5, EtOH); IR (neat) 3365, 2917, 2923, 2856, 2758, 1624, 1413 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.78 (dd, J = 10.5, 5.4 Hz, 1 H), 3.74 −3.63 (m, 2 H), 3.54 (dt, J = 11.6, 7.9 Hz, 1 H), 3.11−3.00 (m, 1 H), 2.61−2.45 (m, 2 H), 2.40−2.30 (m, 1 H), 2.16−1.95 (m, 3 H), 1.81−1.71 (br, 1 H), 1.48−1.35 (m, 1 H);^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 65.1, 64.3, 44.0, 41.1, 38.1, 31.7, 26.9; HRMS (HRFD) m/z: $[M]^+$ Calcd for $C_8H_{13}NO_2$ 155.0946; Found 155.0940.

(1a*S*,6*S*,6a*S*,6b*R*)-6-(((*tert*-Butyldimethylsilyl)oxy) methyl)hexahydro-4*H*-oxireno[2,3-a]-pyrrolizin-4-one (27)

To a stirred solution of olefin **12** (72.0 mg, 0.27 mmol) was added 1,1,1-trifluoroacetone (0.24 mL, 2.69 mmol) in a mixture of acetonitrile (2.70 mL) and EDTA (1.80 mL, 10^{-4} M in water) at 0 °C. A premixed mixture of oxone (0.83 g, 1.35 mmol) and Na_2CO_3 (0.17 g, 2.02 mmol) was added to the above mixture in three portions over 30 min. After being stirred for an additional 0.5 h at 0 °C, the reaction mixture was diluted with water, and the aqueous phase was extracted with dichloromethane (3 × 10 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo* to afford the crude epoxide. The crude epoxide was purified by flash chromatography (eluent: EtOAc) to afford **27** (61.0 mg, 0.22 mmol, 80%). $R_f = 0.54$ (EtOAc); $[\alpha]_D^{21}$ + 3.2 (*c* 1.0, CH_2Cl_2); IR (neat) 3417, 2953, 2929, 2884, 2857, 1704, 1419, 1407, 1360, 1253, 1225, 1112, 1079 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.93 (d, $J = 13.3$ Hz, 1 H), 3.82−3.70 (m, 2 H), 3.64−3.46 (m, 3 H), 2.94 (dd, $J = 13.2$, 0.6 Hz, 1 H), 2.70−2.57 (m, 1 H), 2.39 (dd, $J = 16.4$, 10.2 Hz, 1 H), 2.31 (dd, $J = 16.2$, 9.4 Hz, 1 H), 0.85 (s, 9 H), 0.02 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.1, 64.0, 64.0, 56.1, 55.6, 44.4, 38.5, 36.3, 25.7 (3 C), 18.0, −5.5, −5.6; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{26}NO_3Si$ 284.1682; Found 284.1675.

(+)-Turneforcidine (4)

To a solution containing **27** (24.0 mg, 0.08 mmol) in THF (1.5 mL) was slowly added lithium aluminum hydride (15.0 mg, 0.40 mmol) at 0 °C. The reaction mixture was warmed to room temperature and stirred for 1 h, then was refluxed for 3 h. The reaction was quenched by the addition of three drops of 1 *N* NaOH and two drops of de-ionized water at 0 °C with vigorous stirring for 1 h. The reaction mixture was filtered through a short pad of celite to remove solid, and the solid was washed with methanol (3 × 0.5 mL). The filtrate was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (eluent: DCM/MeOH/NH_4OH, 5/4/1) to give **4** (9.0 mg, 0.06 mmol, 75%) as pale yellow liquid. $R_f = 0.13$ (DCM/ MeOH/ NH_4OH, 5/4/1); $[\alpha]_D^{23}$ + 11.1 (*c* 1.0, MeOH) {Enantiomer Lit [34]. $[\alpha]_D^{20}$ −10.0 (c, 0.8, MeOH)}; IR (neat) 3330, 2940, 2930, 1460, 1156, 1110 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.34 (q, $J = 4.8$ Hz, 1 H), 3.80 (dd, $J = 9.8$, 4.6 Hz, 1 H), 3.46-3.38 (m, 2 H), 3.30 (dd, $J = 8.3$, 5.6 Hz, 1 H), 3.17 (t, $J = 7.4$ Hz, 1 H), 3.05−2.95 (m,1 H), 2.70−2.41 (m, 3 H), 2.10−1.83 (m, 4 H), 1.68−1.53 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 74.2, 71.5, 65.3, 55.0, 52.1, 40.2, 35.4, 30.9; HRMS (HRFI) m/z: $[M]^+$ Calcd for $C_8H_{15}NO_2$ 157.1103; Found 157.1097.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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