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PIDA-promoted intramolecular transannular aziridination to synthesize bridged azatricyclic amines related to methyllycaconitine

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ABSTRACT

A synthetic strategy for the modeling construction of the A/E/F ring system of lycoctonine-type C_{19}-diterpenoid alkaloids bearing a featuring oxygen functional group at C-7 has been successfully developed. The key steps involved a diastereoselective gold(I)-catalyzed annulation to form *cis*-fused cyclopentene and a PIDA-promoted intramolecular transannular aziridination followed by regioselective ring cleavage to give the azatricyclic amine.

1. Introduction

Methyllycaconitine **1** (Fig. 1), a representative member of lycoctonine-type C_{19}-diterpenoid alkaloids,[1] was first extracted from *Delphinium brownii* by Manske in 1938 and later recognized as the principle toxic component.[2,3] Methyllycaconitine acts at the neuromuscular junction, inhibiting neurotransmission and inducing paralysis,[4] and it has been found to be the most potent non-protein antagonist of neuronal nicotinic acetylcholine receptors (nAChRs).[5] Researchers have proposed that methyllycaconitine or analogs therefore could be useful for the treatment of diseases affecting memory or for antiepileptic drug development.[6]

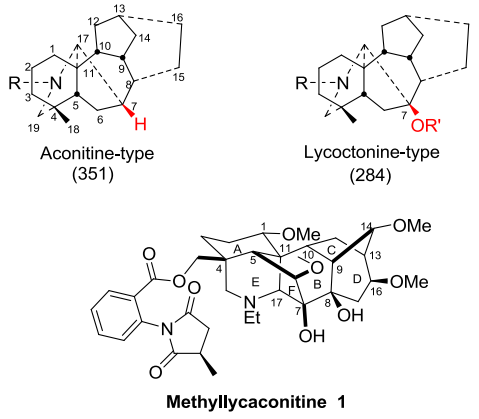

Fig. 1. The structures of C_{19}-diterpenoid alkaloids.

This alkaloid contains a unique and highly strained cage-like skeleton, which includes six rings and 13 stereogenic centers. Its potential medicinal value and intriguingly azahexacyclic structure are very attractive to a number of synthetic chemists.[7] However, synthesis of C_{19}-diterpenoid alkaloid is a conspicuous challenge due to its intricate structure. So far, only three aconitine-type C_{19}-diterpenoid alkaloids have been practically synthesized by the Wiesner and co-workers in 1970s.[8–10] As to the lycoctonine-type C_{19}-diterpenoid alkaloids (about 280 natural compounds), which differ from aconitine-type alkaloids (about 350 natural compounds) in the substitution pattern at C-7 and possess an extra oxygen-containing functionality at this position (Fig. 1),[1] no chemical preparation of any member of lycoctonine-type alkaloids has been described. Although several partial ring systems, such as A/E,[11–18] A/E/F,[19] and A/B/E/F[20] subunits have been reported in the synthesis toward methyllycaconitine in the past decades, none of these systems has been constructed with the featuring C-7 oxygen function. In collection with our long-standing interests toward the total synthesis of C_{19}-diterpenoid alkaloids,[21,22] we planned to develop a new and efficient methodology for constructing the A/E/F

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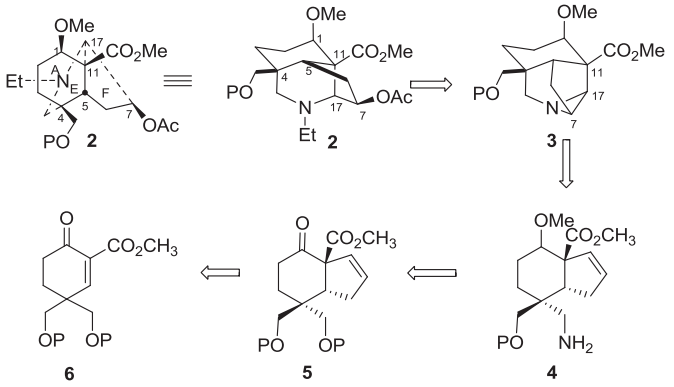
ring system with a key C-7 oxygen substituent, which would be one of the crucial points for the total synthesis the lycoctonine-type C_{19}-diterpenoid alkaloids. We now describe a novel synthetic procedure leading to tricyclic amine **2** as the model for A/E/F ring system of methyllycaconitine using an intramolecular transannular aziridination and a subsequent regioselective ring cleavage as the key steps.

2. Results and discussion

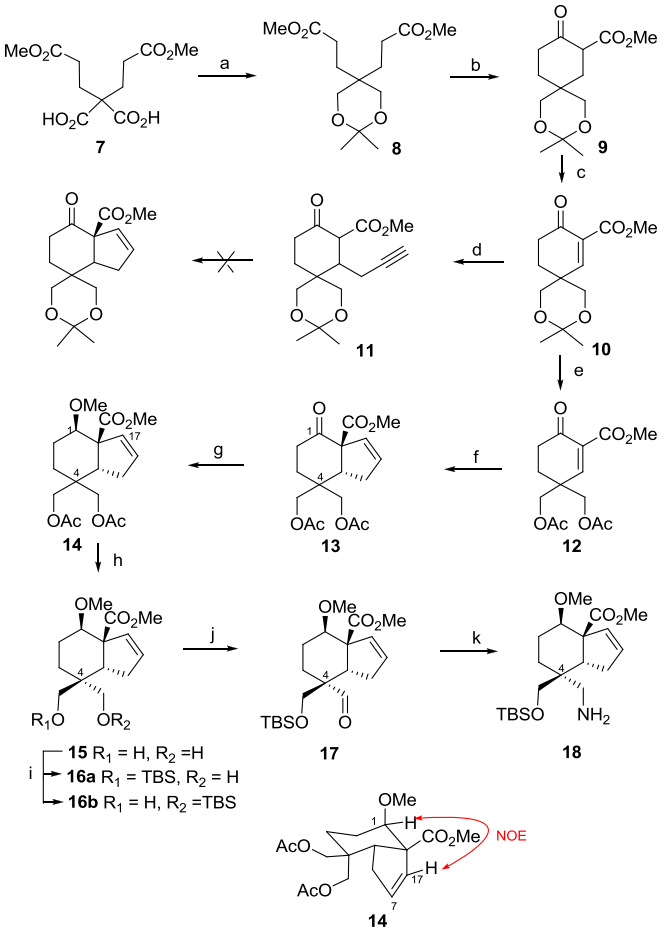
The retrosynthetic analysis (Scheme 1) involved an initial C–N bond connection from **2** to a bridged, polycyclic aziridine **3**, which could be expected to arise from a transannular intramolecular aziridination by oxidation of unsaturated primary amine **4**. Appropriate functional group interconversions suggest that **4** could be derivable from ketone **5**. In turn, the bicycle A/F ring could be assembled by a cyclopentene annulation onto α,β-unsaturated ketoester **6**.



Scheme 1. Retrosynthetic analysis for A/E/F ring **2** (P=protecting group).

Our synthesis began with the known 2,2-bis(3-methoxy-3-oxopropyl) malonic acid **7** (Scheme 2), readily available in two steps from dibenzyl malonate.[23] Selectively reduction of malonic acid function with BH_3[24] followed by protection of resulting 1,3-diol furnished the acetonide **8**. Then Dieckmann condensation[25] by treatment of **8** with potassium *tert*-butoxide in THF afforded the β-ketoester **9** in 95% yield. Oxidation of **9** with DDQ in 1,4-dioxane gave the conjugate enone **10** smoothly.[26,27] With the enone ester in hand, the crucial cyclopentene annulation was attempted. Toste et al. had found with the similar substrate an efficient conjugate addition of allenyltriphenylstannane followed by gold(I)-catalyzed cyclization of resulting acetylenic β-ketoester afforded *cis*-fused cyclopentene as a single diastereomer.[28] In this case, the first step for introduction of propargyl group by conjugate addition of **10** with allenyltriphenylstannane in presence of $TiCl_4$ was partially successful, presumably due to the presence of acid sensitive acetonide group in **10**. **11** was isolated, but only in 30% yield. The following annulation of **11** under the Toste's gold-catalysis condition was also totally failed. These factors led us to reconsider the appropriateness of the acetonide protecting group. Thus, direct acetylation of the spiroketal group with catalytic $FeCl_3$ in AcOH[30] gave diacetyl ester **12** in 96% yield. With this substrate, the conjugate propargylation[29] and the following gold(I)-catalyzed cyclization by Toste's procedure[28] proceeded smoothly, delivering the cyclopentene **13** as a single diastereomer in 87% yield over two steps.

With the key A/F ring precursor in place, we then turned our attention to installation of methoxy group at C-1 and realization of the C-4 quaternary stereocenter by desymmetrization of the prochiral diol (Scheme 2). Accordingly, reduction of ketone **13** with

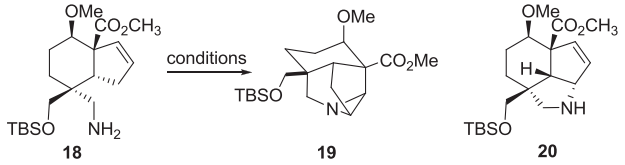


Scheme 2. Synthesis of intermediate **18**. Reagents and conditions: (a) (i) $BH_3{\cdot}SMe_2$, THF, (ii) $(CH_3)_2CH(OCH_3)_2$, *p*-TsOH, Tol, 75% for two steps; (b) ^tBuOK, THF, 95%; (c) DDQ, 1,4-dioxane, 89%; (d) $TiCl_4$, allenyltriphenylstannane, CH_2Cl_2, 30%; (e) $FeCl_3{\cdot}6H_2O$, Ac_2O, AcOH, 96%; (f) (i) $TiCl_4$, allenyltriphenylstannane, CH_2Cl_2, 87%, (ii) cat. $AuCl(PPh_3)$, cat. AgOTf, CH_2Cl_2, 100%; (g) (i) $NaBH_4$, CH_3OH, 95%, (ii) Ag_2O, CH_3I, SMe_2, 4 Å MS, THF, 88%; (h) K_2CO_3, CH_3OH, 98%; (i) TBSCl, Et_3N, DMAP, DMF, **16a** (70%), and **16b** (23%); (j) PCC, Na_2CO_3, 4 Å MS, CH_2Cl_2, 92%; (k) $Ti(O^iPr)_4$, NH_3/EtOH, then $NaBH_4$, 85%.

$NaBH_4$ in MeOH, followed by methylation with MeI/Ag_2O gave the exclusive C-1 β-methoxy product **14** in 84% yield over two steps.[31] The stereochemistry of C-1 methoxy group was assigned as β orientation based on NOE difference experiment, which shows through-space interaction between H-1 (3.14 ppm) and olefin proton H-17 (6.03 ppm). This stereochemistry presumably arises due to the kinetic attack of hydride from the less encumbered α face (the β face was seriously hindered by the ester group). After removal of the acetyl group of **14** under basic condition, regioselective monoprotection of resulting 1,3-diol was effected by treatment with TBSCl/TEA/DMAP in DMF, delivering the silyl ether on the β-face to give **16a** as the major product in 70% yield, along with 23% yield of separable diastereoisomer **16b**. The unwanted **16b** could be easily recycled to diol **15** by treatment with TBAF in THF. The relatively good regioselectivity of this reaction could be attributed to the more severe steric hindrance of α-face caused by the fused cyclopentene moiety than that of β-face. The remaining primary alcohol in **16a** was then oxidized with PCC/Na_2CO_3 in dichloromethane to furnish an aldehyde **17**, which subsequently underwent reductive amination by treatment with ammonia in ethanol and titanium (IV) isopropoxide, followed by reduction in situ with $NaBH_4$, affording primary amine **18** in 85% yield.[32]

With the key intermediate **18** in hand, our effort was focused on the construction of the challenging bridged polycyclic aziridine. As shown in Table 1, initial attempt to direct cyclization of **18** by the

Table 1
Intramolecular transannular aziridination of primary amine **18**



Entry	Conditions	Yield of **19** (%)
1	$Pb(OAc)_4$ (2 equiv), K_2CO_3 (4 equiv), PhH, rt→60 °C	0[a]
2	NCS (2 equiv), CH_2Cl_2, rt, 12 h	0[b]
3	NBS (2 equiv), acetone, rt, 2 h	10
4	NBS (2 equiv), DMF, rt, 2 h	30[c]
5	NBA (2 equiv), DMF, rt, 2 h	24[c]
6	NIS (2 equiv), DMF, rt, 2 h	20[c]
7	PIDA (2 equiv), K_2CO_3 (2 equiv), DCE, 50 °C, 2 h	40
8	PIDA (2 equiv), MgO (2 equiv), DCE, 50 °C, 2 h	33
9	PIDA (2 equiv),$Cu(OTf)_2$, (0.5 equiv), DCE, 50 °C, 2 h	35
10	**PIDA (1.2 equiv), K_2CO_3 (2 equiv), SiO_2, DCE, 50 °C, 1 h**	**70**
11	PIFA (1.2 equiv), K_2CO_3 (2 equiv), SiO_2, DCE, 50 °C, 1 h	38

Significance of bold value indicates that the condition in entry 10 is the best result.
[a] All of the amine **18** was recovered.
[b] Mono- or di-chloramine was observed.
[c] With almost same amount of byproduct **20** was isolated.

Nagata's intramolecular aziridination method[33,34] (entry 1) was unsuccessful. Treatment of **18** with NCS still did not afford the desired product, yielding only fairly stable mono- or di-chloramine (entry 2). Encouragingly, when applying NBS in acetone, a small amount of desired aziridine **19** was isolated from the reaction mixture (entry 3).[35] Further optimization of reaction conditions provided aziridine in up to 30% yield (entry 4), but with almost same quantities of major allylic amination byproduct **20** and some unidentified low polar compounds. Screening of other halogenated reagents, such as *N*-bromoacetamide (NBA) and *N*-iodosuccinimide (NIS) got worse results (entry 5 and 6). It has been widely reported that the hypervalent iodine reagents could promote nitrene transfer to olefin giving aziridine in high yields,[36–38] despite mostly using electron withdrawing group substituted amine, such as sulfonamides[39] or carbamates[40] as substrates. To our delight, when **18** was treated with phenyliodine(III) diacetate (PIDA) and K_2CO_3 in 1,2-dichloroethane at 50 °C for 2 h, **19** was obtained in 40% yield without allylic amination byproduct found (entry 7). After a series of experiments (entry 8–10), we found that treatment of **18** with PIDA and K_2CO_3 using silica gel as additive gave the best result (entry 10), delivering **19** in up to 70% yield. To the best of our knowledge, it was the first time that PIDA was used as a sole promoter for intramolecular aziridination of primary amine. Additionally, the use of more potent oxidant phenyliodine(III) bistrifluoroacetate (PIFA) resulted in lower yield (entry 11). It is worthy to note that the aziridine **19** is fairly stable and could be stored at rt even at neat liquid state. The structure of **19** was further confirmed by single-crystal X-ray analysis of the corresponding methyl quaternary amine salt (Fig. 2).

Having achieved the synthesis of bridged aziridine, regioselective ring cleavage and installation of oxygen function at C-7 were next addressed (Scheme 3). Initial treatment of **19** with acetic anhydride in dichloromethane provided a 2:1 inseparable mixture of regioisomers **21a** and **21b** in which the desired product **21a** could be identified as the major isomer by the ^1H NMR spectrum.[41] Pleasingly, reaction with ethyl iodide in DMF at rt generated a more reactive quaternary amine salt, which was in turn treated with sodium acetate in one pot at an elevated temperature, providing a 3.8:1 separable mixture of regioisomers **22a** and **22b** from which the desired major isomer **22a** was isolated in 77% yield. The structure of **22a** was further unambiguously established by its X-ray crystallography.

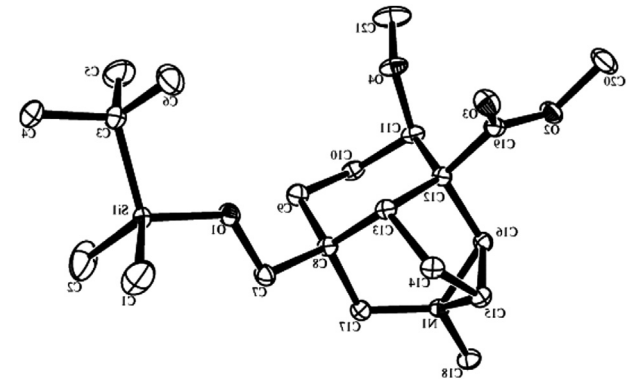
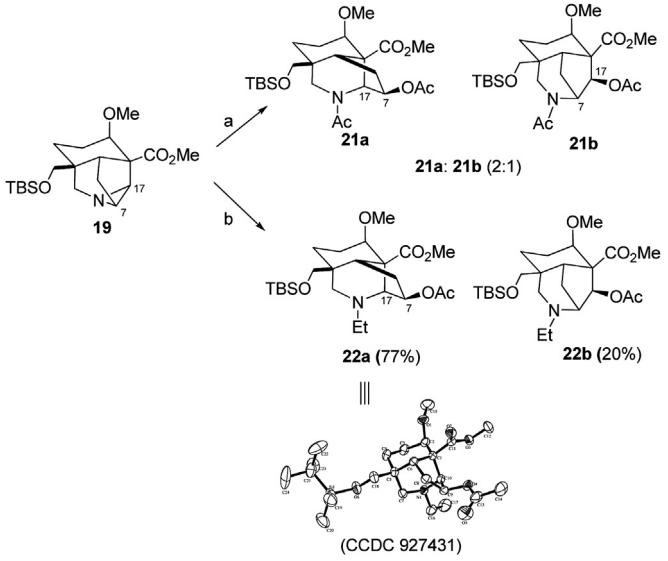


Fig. 2. ORTEP diagram from the X-ray crystal structure of methyl quaternary amine salt of **19** (CCDC 927430).



Scheme 3. Regioselective ring cleavage of aziridine **19**. Reagents and conditions: (a) Ac_2O, CH_2Cl_2, 90%, inseparable; (b) EtI, DMF, then NaOAc **22a** (77%), **22b** (20%).

3. Conclusion

In conclusion, the synthesis of desired tricyclic amine **22a** modeling the A/E/F ring system of lycoctonine-type C_{19}-diterpenoid alkaloids has been successfully accomplished by using gold(I)-catalyzed annulation reaction and unprecedented PIDA-promoted transannular aziridination of primary amine followed by regioselective ring cleavage as the key steps. The development of this methodology thus should provide a basis for the total synthesis of methyllycaconitine.

4. Experimental section

4.1. General information

Melting points were determined on a Kofler block (uncorrected); IR spectra were recorded on a Nicolet 200 SXV spectrometer; HRMS were obtained with a Bruker BioTOFQ mass spectrometer; ^1H and ^{13}C NMR spectra were acquired on a Varian INOVA-400/54 spectrometer, with TMS as internal standard; Silica gel GF_{254} and H (10–40 mm, Qingdao Marine Chemical Factory, China) were used for TLC and CC. Tetrahydrofuran (THF) was freshly distilled from sodium/benzophenone. Unless otherwise noted, all reactions were carried out under an atmosphere of argon or nitrogen.

4.2. Preparation of acetonide 8

To a stirred solution of 2,2-bis(3-methoxy-3-oxopropyl) malonic acid (16.6 g, 60 mmol) in THF (500 mL) at 0 °C was added dropwise $BH_3 \cdot SMe_2$ (10.7 g, 70.5 mmol). The reaction mixture was slowly warmed to 25 °C and stirred overnight. Then 80 mL CH_3OH was added dropwise to quench the reaction and the mixture was concentrated in vacuo. The resultant residue was dissolved in 200 mL toluene and TsOH (516 mg, 3 mmol), 2,2-dimethoxypropane (12.5 g, 0.12 mol) were added in one portion. After being stirred at rt for 8 h, the reaction was quenched with std $NaHCO_3$ solution and the organic layer was washed with brine, dried over $MgSO_4$, concentrated to give a residue, which was purified by silica gel chromatography with PE/EtOAc (20:1) to give acetonide **8** (13.0 g, 75% for two steps). Colorless oil; IR (film) ν_{max}: 2951, 2869, 1738, 1438, 1375, 1202, 1085 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.68 (s, 6H), 3.57 (s, 4H), 2.39–2.19 (m, 4H), 1.79–1.60 (m, 4H), 1.40 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 97.7, 66.9, 51.2, 33.7, 27.5, 26.7, 23.2; HRMS (ESI) calcd for $C_{14}H_{24}NaO_6^+$ $[M+Na]^+$ 311.1471, found 311.1469.

4.3. Preparation of β-ketoester 9

To a stirred solution of **8** (13.7 g, 47.5 mmol) in THF (300 mL) at −20 °C was added ^tBuOK (6.4 g, 57 mmol). The reaction was completed in 1.5 h and quenched with std NH_4Cl solution. The layers were separated, and the aqueous layer was extracted with EtOAc. The combined organics were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The crude residue was purified by silica gel chromatography with PE/EtOAc (30:1) to yield β-ketoester **9** (11.5 g, 95%). White solid; mp: 67–69 °C; IR (KBr) ν_{max}: 3422, 2945, 2856, 1666, 1614, 1448, 1357, 1280, 1222, 1058 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 12.16 (s, 1H), 3.76 (s, 3H), 3.61 (s, 4H), 2.32 (t, J=6.7 Hz, 2H), 2.18 (s, 2H), 1.69 (t, J=6.7 Hz, 2H), 1.44 (s, 3H), 1.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 170.6, 98.2, 94.8, 67.6, 51.3, 31.3, 28.2, 25.9, 24.9, 23.8, 23.2; HRMS (ESI) calcd for $C_{13}H_{20}NaO_5^+$ $[M+Na]^+$ 279.1208, found 279.1213.

4.4. Preparation of ene-ketoester 10

To a solution of **9** (7.2 g, 28 mmol) in 1,4-dioxane (140 mL) was added DDQ (6.7 g, 29.5 mmol), and the mixture was stirred at rt for 1 h. Then hexane (200 mL) was added and the solid filtered. The filtrate was concentrated to give a residue, which was dissolved in CH_2Cl_2 and washed with 5% $NaHCO_3$ solution, and the aqueous layer was extracted with CH_2Cl_2. The combined organics were dried on Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel chromatography with PE/EtOAc (3:1) to yield ene-ketoester **10** (6.3 g, 89%). White solid; mp: 100–102 °C; IR (KBr) ν_{max}: 2952, 2873, 1732, 1675, 1380, 1366, 1267, 1076, 1034 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.63 (s, 1H), 3.86 (d, J=11.8 Hz, 2H), 3.82 (s, 3H), 3.78 (d, J=11.8 Hz, 2H), 2.53 (t, J=6.9 Hz, 2H), 2.00 (t, J=6.9 Hz, 2H), 1.49 (s, 3H), 1.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.5, 164.5, 156.1, 132.6, 98.4, 66.2, 52.0, 36.2, 33.8, 27.1, 23.7, 22.8; HRMS (ESI) calcd for $C_{13}H_{18}NaO_5^+$ $[M+Na]^+$ 277.1052, found 277.1050.

4.5. Preparation of alkyne 11

To a stirred solution of **10** (203 mg, 0.8 mmol) in CH_2Cl_2 (5 mL) at −78 °C was added dropwise a solution of $TiCl_4$ (0.96 mL, 1 M in CH_2Cl_2, 0.96 mmol). After 10 min, a solution of allenyltriphenylstannane (467 mg, 1.2 mmol) in 1.2 mL CH_2Cl_2 was added. The mixture was allowed to reach rt gradually and stirred for another 2 h. The reaction was quenched with 4 mL water and extracted with CH_2Cl_2. The combined organics were dried over Na_2SO_4, concentrated, and then taken up in 6 mL Et_2O and treated with 3 mL std KF solution. The resulting suspension was stirred at rt for 1 h, filtered, and extracted with EtOAc. The combined organics were dried over $MgSO_4$, concentrated to yield a residue, which was purified by silica gel chromatography with PE/EtOAc (8:1) to yield alkyne **11** (70 mg, 30%). Colorless oil; IR (film) ν_{max}: 2934, 1733, 1649, 1476 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 12.51 (s, 1H), 3.78 (s, 3H), 3.60–3.52 (m, 2H), 3.51–3.38 (m, 2H), 2.81 (d, J=4.7 Hz, 1H), 2.61–2.49 (m, 1H), 2.46–2.38 (m, 2H), 2.38–2.29 (m, 2H), 1.95 (s, 1H), 1.72–1.61 (m, 1H), 1.31 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 172.7, 98.4, 83.5, 80.7, 70.8, 68.8, 67.2, 51.5, 40.0, 30.8, 25.4, 25.0, 24.6, 21.2, 20.3; HRMS (ESI) calcd for $C_{16}H_{22}NaO_5^+$ $[M+Na]^+$ 317.1365, found 317.1358.

4.6. Preparation of diacetyl ester 12

To a stirred solution of **10** (7.0 g, 27.6 mmol) in AcOH (55 mL) was added $FeCl_3 \cdot 6H_2O$ (2.2 g, 8.3 mmol). After 2 h, Ac_2O (11 mL) was added and stirring was maintained for another 3 h. Then EtOAc (600 mL) was added and the organics were washed successively with H_2O (2×150 mL), std $NaHCO_3$ solution (2×100 mL), and dried over $MgSO_4$, concentrated to give a residue, which was purified by silica gel chromatography with PE/EtOAc (4:1) to yield diacetyl ester **12** (7.9 g, 96%). White solid; mp: 81–83 °C; IR (KBr) ν_{max}: 2958, 2854, 1743, 1686, 1367, 1236, 1042 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.23 (d, J=11.3 Hz, 2H), 4.08 (d, J=11.3 Hz, 2H), 3.83 (s, 3H), 2.62 (t, J=6.8 Hz, 2H), 2.10 (s, 6H), 2.02 (t, J=6.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.1, 170.3, 164.4, 153.1, 134.3, 64.8, 52.4, 40.2, 34.0, 26.1, 20.6; HRMS (ESI) calcd for $C_{14}H_{18}NaO_7^+$ $[M+Na]^+$ 321.0950, found 321.0954.

4.7. Preparation of cyclopentene 13

To a stirred solution of **12** (6.2 g, 20.8 mmol) in CH_2Cl_2 (130 mL) at −78 °C was added dropwise a solution of $TiCl_4$ (27 mL, 1 M in CH_2Cl_2, 27 mmol). After 10 min, a solution of allenyltriphenylstannane (12.1 g, 31.2 mmol) in 40 mL CH_2Cl_2 was added. The mixture was allowed to reach rt gradually and stirred for another 2 h. The reaction was quenched with 80 mL water and extracted with CH_2Cl_2. The combined organics were dried over Na_2SO_4, concentrated, and then taken up in 150 mL Et_2O and treated with 75 mL std KF solution. The resulting suspension was stirred at rt for 1 h, filtered, and extracted with EtOAc. The combined organics were dried over $MgSO_4$, concentrated to yield a residue, which was purified by silica gel chromatography with PE/EtOAc (10:1) to yield an intermediate **12S** (6.1 g, 87%). White solid; mp: 57–59 °C; IR (KBr) ν_{max}: 3281, 2954, 1740, 1653, 1615, 1441, 1238, 1043 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 12.46 (s, 1H), 4.17 (d, J=11.5 Hz, 1H), 4.01 (d, J=11.5 Hz, 1H), 3.96 (s, 2H), 3.80 (s, 3H), 2.69 (s, 1H), 2.57 (ddd, J=17.5, 5.5, 2.3 Hz, 1H), 2.45–2.23 (m, 3H), 2.22–2.12 (m, 1H), 2.09 (s, 3H), 2.06 (s, 3H), 1.96 (s, 1H), 1.66–1.55 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 172.0, 170.7, 170.6, 97.8, 82.2, 70.8, 65.2, 63.4, 51.4, 38.6, 33.0, 24.8, 20.6, 20.1; HRMS (ESI) calcd for $C_{17}H_{22}NaO_7^+$ $[M+Na]^+$ 361.1263, found 361.1274.

To a solution of intermediate **12S** (2.6 g, 7.7 mmol) in CH_2Cl_2 (50 mL) were added $AuCl(PPh_3)$ (38 mg, 0.077 mmol) and AgOTf (20 mg, 0.077 mmol). The reaction mixture was stirred at rt for 6 h, then concentrated. The residue was directly purified by silica gel chromatography with PE/EtOAc (5:1) to give cyclopentene **13** (2.6 g, 100%). White solid; mp: 64–66 °C; IR (KBr) ν_{max}: 2955, 1743, 1703, 1441, 1384, 1222, 1040 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.99 (d, J=5.4 Hz, 1H), 5.86 (d, J=5.4 Hz, 1H), 4.24 (d, J=11.6 Hz, 1H), 4.18 (d, J=11.6 Hz, 1H), 4.05 (d, J=11.4 Hz, 1H), 3.91 (d, J=11.4 Hz, 1H), 3.77 (s, 3H), 3.14 (t, J=8.6 Hz, 1H), 2.74–2.59 (m, 1H), 2.52 (dd, J=16.4, 8.6 Hz, 1H), 2.44–2.29 (m, 2H), 2.09 (s, 3H), 2.06 (s, 3H), 1.98–1.84 (m, 1H), 1.81–1.70 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$)

δ 207.3, 172.5, 170.4, 170.4, 132.9, 130.5, 68.8, 65.7, 64.1, 53.0, 47.1, 38.0, 34.3, 33.3, 24.8, 20.5; HRMS (ESI) calcd for $C_{17}H_{22}NaO_7^+$ $[M+Na]^+$ 361.1263, found 361.1274.

4.8. Preparation of methyl ether 14

To a solution of **13** (2.9 g, 8.7 mmol) in MeOH (145 mL) at 0 °C was added $NaBH_4$ (395 mg, 10.4 mmol). After being stirred for 1 h, the reaction was quenched with std NH_4Cl solution. The mixture was extracted with CH_2Cl_2 and the combined organics were dried over Na_2SO_4, concentrated to give a residue, which was purified by silica gel chromatography with PE/EtOAc (2:1) to give an intermediate **13S** (2.8 g, 95%). Colorless oil; IR (film) ν_{max}: 3526, 2950, 1739, 1367, 1241, 1046 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.07 (d, J=5.5 Hz, 1H), 6.00 (d, J=5.5 Hz, 1H), 4.05–3.91 (m, 3H), 3.81 (d, J=11.1 Hz, 1H), 3.75 (s, 3H), 3.65 (d, J=11.7 Hz, 1H), 3.39 (td, J=11.7, 4.2 Hz, 1H), 2.83 (t, J=9.7 Hz, 1H), 2.47–2.24 (m, 2H), 2.07 (s, 3H), 2.06 (s, 3H), 1.95–1.68 (m, 3H), 1.40 (td, J=13.7, 3.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 170.7, 170.5, 136.2, 131.3, 75.8, 67.1, 63.3, 59.2, 52.3, 47.5, 38.2, 32.1, 26.9, 25.3, 20.8, 20.7; HRMS (ESI) calcd for $C_{17}H_{24}NaO_7^+$ $[M+Na]^+$ 363.1420, found 363.1414.

To a solution of intermediate **13S** (2.0 g, 6.0 mmol) in THF (80 mL) at rt were added successively 4 Å MS (3.0 g), Ag_2O (6.9 g, 30 mmol), Me_2S (2.2 mL, 30 mmol), and CH_3I (7.5 mL, 0.12 mol). The resulting suspension was kept in dark place and stirred overnight, then filtered over a pad of silica, washed with EtOAc, and concentrated to give a residue, which was directly purified by silica gel chromatography with PE/EtOAc (5:1) to give methyl ether **14** (1.9 g, 88%). Colorless oil; IR (film) ν_{max}: 2946, 2828, 1740, 1457, 1436, 1368, 1240, 1103, 1045 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.03 (d, J=5.5 Hz, 1H), 5.87 (d, J=5.5 Hz, 1H), 4.34 (d, J=11.3 Hz, 1H), 4.14 (d, J=11.3 Hz, 1H), 4.03 (d, J=11.1 Hz, 1H), 3.81 (d, J=11.1 Hz, 1H), 3.71 (s, 3H), 3.33 (s, 3H), 3.14 (d, J=8.0 Hz, 1H), 2.66 (t, J=9.1 Hz, 1H), 2.47–2.27 (m, 2H), 2.15–1.95 (m, 1H), 2.04 (s, 6H), 1.74 (d, J=10.8 Hz, 2H), 1.37–1.21 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.3, 170.7, 170.4, 136.1, 129.7, 83.7, 67.1, 64.0, 60.4, 57.6, 51.7, 45.7, 37.9, 33.3, 23.8, 20.7; HRMS (ESI) calcd for $C_{18}H_{26}NaO_7^+$ $[M+Na]^+$ 377.1576, found 377.1568.

4.9. Preparation of diol 15

To a solution of **14** (2.6 g, 7.2 mmol) in MeOH (120 mL) at 0 °C, was added K_2CO_3 (2.5 g, 18 mmol). After being stirred for 2 h, the reaction was quenched with 1 N HCl solution (40 mL). The mixture was concentrated to about 30 mL, then diluted with water, and extracted with EtOAc. The combined organics were dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by silica gel chromatography with PE/EtOAc (1:1) to yield diol **15** (1.9 g, 98%). Colorless oil; IR (film) ν_{max}: 3419, 2944, 1729, 1456, 1437, 1253, 1099, 1047 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.84 (d, J=5.3 Hz, 1H), 5.77 (d, J=5.3 Hz, 1H), 4.28 (d, J=11.8 Hz, 1H), 4.06 (s, 1H), 3.87 (s, 1H), 3.76 (s, 3H), 3.67 (d, J=10.6 Hz, 1H), 3.54 (d, J=10.6 Hz, 1H), 3.44 (d, J=11.8 Hz, 1H), 3.32 (d, J=3.8 Hz, 1H), 3.25 (s, 3H), 3.18 (t, J=9.2 Hz, 1H), 2.68 (dd, J=16.7, 9.0 Hz, 1H), 2.29 (dd, J=16.7, 9.5 Hz, 1H), 1.79 (ddd, J=14.8, 10.1, 5.0 Hz, 1H), 1.44–1.31 (m, 1H), 1.04 (dd, J=8.8, 4.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.1, 133.9, 131.3, 81.4, 72.7, 69.0, 62.0, 57.0, 51.9, 39.5, 38.2, 35.0, 22.0, 19.7; HRMS (ESI) calcd for $C_{14}H_{22}NaO_5^+$ $[M+Na]^+$ 293.1365, found 293.1368.

4.10. Preparation of silyl ether 16a and 16b

To a solution of **15** (2.0 g, 7.4 mmol) in DMF (25 mL) at 0 °C were added Et_3N (1.5 mL, 11.1 mmol), DMAP (450 mg, 3.7 mmol), and TBSCl (1.2 g, 7.8 mmol). The mixture was warmed to rt and stirred for 2 h. Then EtOAc (200 mL) was added and the organics were washed with brine (3×50 mL), and dried over $MgSO_4$, concentrated in vacuo. The residue was purified by silica gel chromatography with PE/EtOAc (10:1–3:1) to yield silyl ether **16a** (2.0 g, 70%) and **16b** (650 mg, 23%). Data for **16a**: colorless oil; IR (film) ν_{max}: 3411, 2932, 2856, 1726, 1466, 1437, 1254, 1099, 1047 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.03 (d, J=5.3 Hz, 1H), 5.89 (d, J=5.3 Hz, 1H), 3.93 (d, J=9.8 Hz, 1H), 3.73 (d, J=9.8 Hz, 2H), 3.68 (s, 3H), 3.58 (dd, J=10.6, 4.2 Hz, 1H), 3.49 (dd, J=10.6, 6.4 Hz, 1H), 3.33 (s, 3H), 3.24 (t, J=5.4 Hz, 1H), 3.10 (dd, J=10.8, 3.9 Hz, 1H), 2.65 (t, J=9.0 Hz, 1H), 2.55 (dd, J=15.2, 8.2 Hz, 1H), 2.30 (dd, J=15.2, 10.3 Hz, 1H), 2.10–1.89 (m, 1H), 1.81–1.70 (m, 1H), 1.71–1.60 (m, 1H), 1.36–1.22 (m, 1H), 0.89 (s, 9H), 0.09 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 136.2, 130.2, 84.9, 71.4, 68.6, 60.2, 57.8, 51.6, 45.8, 39.8, 33.3, 25.7, 24.4, 21.3, 17.9, −5.7, −5.9; HRMS (ESI) calcd for $C_{20}H_{37}O_5Si^+$ $[M+H]^+$ 385.2410, found 385.2410.

Data for **16b**: white solid; mp: 55–57 °C; IR (KBr) ν_{max}: 3521, 2928, 2855, 1733, 1470, 1254, 1094 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.02 (d, J=5.3 Hz, 1H), 5.88 (d, J=5.3 Hz, 1H), 3.81 (dd, J=11.1, 6.7 Hz, 1H), 3.72 (s, 3H), 3.61 (dd, J=11.1, 5.0 Hz, 1H), 3.55 (d, J=9.5 Hz, 1H), 3.45 (d, J=9.5 Hz, 1H), 3.32 (s, 3H), 3.09 (dd, J=10.2, 3.6 Hz, 1H), 2.93 (t, J=6.0 Hz, 1H), 2.80 (t, J=9.4 Hz, 1H), 2.39 (dd, J=15.2, 8.5 Hz, 1H), 2.33–2.19 (m, 1H), 2.12–1.92 (m, 1H), 1.75–1.61 (m, 1H), 1.48 (dt, J=13.7, 4.5 Hz, 1H), 1.32–1.19 (m, 1H), 0.89 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 136.1, 130.3, 84.1, 70.7, 65.9, 60.7, 57.6, 51.8, 44.1, 39.9, 33.5, 25.7, 23.8, 21.0, 18.0, −5.8, −5.9; HRMS (ESI) calcd for $C_{20}H_{37}O_5Si^+$ $[M+H]^+$ 385.2410, found 385.2410.

4.11. Preparation of aldehyde 17

To a stirred solution of **16a** (1.2 g, 3.1 mmol) in CH_2Cl_2 (30 mL) were added 4 Å MS (2.4 g), Na_2CO_3 (660 mg, 6.2 mmol), and PCC (1.3 g, 6.2 mmol) at 0 °C. After 10 min, the ice bath was removed and stirring was continued for 1 h at rt. Then ether (60 mL) was added and the mixture was filtered over a pad of silica, washed with ether. The filtrate was concentrated in vacuo to give a residue, which was purified by silica gel chromatography with PE/EtOAc (30:1) to yield aldehyde **17** (1.1 g, 92%). Colorless oil; IR (film) ν_{max}: 2932, 2857, 1734, 1466, 1254, 1207, 1100 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.53 (s, 1H), 5.87 (d, J=5.6 Hz, 1H), 5.81 (d, J=5.6 Hz, 1H), 3.93 (d, J=10.1 Hz, 1H), 3.87 (d, J=10.1 Hz, 1H), 3.70 (s, 3H), 3.43–3.34 (m, 1H), 3.31 (s, 3H), 2.81 (t, J=7.3 Hz, 1H), 2.45 (dd, J=16.5, 7.8 Hz, 1H), 2.26 (dd, J=16.5, 6.8 Hz, 1H), 2.01–1.88 (m, 1H), 1.87–1.77 (m, 1H), 1.73–1.57 (m, 2H), 0.85 (s, 9H), 0.03 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.6, 173.6, 134.7, 131.3, 81.8, 66.4, 62.4, 57.2, 51.8, 42.8, 34.6, 25.7, 20.4, 19.3, 18.1, −5.6, −5.7; HRMS (ESI) calcd for $C_{20}H_{34}NaO_5Si^+$ $[M+Na]^+$ 405.2073, found 405.2068.

4.12. Preparation of primary amine 18

To a solution of **17** (575 mg, 1.5 mmol) in std NH_3/EtOH solution (130 mL) at 0 °C was added $Ti(O^iPr)_4$ (470 mg, 1.65 mmol). The mixture was warmed to rt and stirred for 3 h. Then $NaBH_4$ (113 mg, 3 mmol) was added and stirring was continued for another 30 min. The reaction was then quenched with 20 mL concd ammonia solution. The resulting precipitate was filtered and the filtrate was concentrated to about 30 mL, then diluted with water and extracted with EtOAc. The organics were dried over $MgSO_4$ and concentrated. The residue was purified by silica gel chromatography with $CHCl_3$/CH_3OH (20:1) to give amine **18** (490 mg, 85%). Colorless oil; IR (film) ν_{max}: 3396, 2931, 2855, 1735, 1465, 1253, 1198, 1097 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.05 (d, J=5.2 Hz, 1H), 5.88 (s, 1H), 3.75 (d, J=10.1 Hz, 1H), 3.68 (s, 3H), 3.53 (d, J=10.1 Hz, 1H), 3.33 (s, 3H), 3.04 (d, J=8.8 Hz, 1H), 2.70 (d, J=13.0 Hz, 1H), 2.55–2.46 (m, 2H), 2.44–2.35 (m, 1H), 2.35–2.24 (m, 1H), 2.03 (q, J=12.0 Hz, 1H), 1.75 (d, J=11.0 Hz, 2H), 1.13 (t, J=11.5 Hz, 1H), 0.89 (s, 9H), 0.06 (s, 3H),

0.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 137.0, 130.0, 85.4, 63.2, 60.1, 57.9, 51.6, 47.9, 40.5, 33.2, 25.8, 25.6, 21.6, 18.0, −5.6, −5.7; HRMS (ESI) calcd for $C_{20}H_{38}NO_4Si^+$ $[M+H]^+$ 384.2570, found 384.2573.

4.13. Preparation of aziridine 19 with NBS/DMF

To a solution of **18** (153 mg, 0.40 mmol) in DMF (2 mL) at rt was added NBS (142 mg, 0.80 mmol). The mixture was stirred for 2 h, then quenched with 20 mL std $Na_2S_2O_3$ solution and extracted with EtOAc. The combined organics were dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by silica gel chromatography with PE/EtOAc (1:1–1:2) to yield aziridine **19** (45 mg, 30%) and byproduct **20** (42 mg, 28%). Data for **19**: colorless oil; IR (film) ν_{max}: 2928, 2854, 1741, 1465, 1250, 1091 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.95 (s, 1H), 3.72 (s, 3H), 3.40 (d, J=9.7 Hz, 1H), 3.28 (s, 3H), 3.25 (d, J=9.7 Hz, 1H), 2.87 (s, 2H), 2.51 (s, 1H), 2.33 (s, 1H), 2.14 (d, J=5.1 Hz, 1H), 2.06–1.97 (m, 2H), 1.86 (t, J=14.4 Hz, 1H), 1.77 (dd, J=13.3, 5.0 Hz, 1H), 1.44 (td, J=13.6, 3.2 Hz, 1H), 1.29–1.15 (m, 1H), 0.87 (s, 9H), 0.02 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 79.0, 69.7, 56.8, 55.8, 51.8, 49.4, 39.4, 37.2, 33.0, 31.5, 28.1, 25.9, 25.2, 20.4, 18.3, −5.5; HRMS (ESI) calcd for $C_{20}H_{36}NO_4Si^+$ $[M+H]^+$ 382.2414, found 382.2346.

Data for **20**: colorless oil; IR (film) ν_{max}: 2935, 2821, 1755, 1487 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.65 (d, J=5.2 Hz, 1H), 5.57 (d, J=5.2 Hz, 1H), 4.59 (d, J=6.7 Hz, 1H), 3.83 (d, J=3.7 Hz, 1H), 3.69 (s, 3H), 3.42 (d, J=9.3 Hz, 1H), 3.32 (d, J=9.3 Hz, 1H), 3.26 (s, 3H), 2.95 (d, J=6.7 Hz, 1H), 2.88 (d, J=12.0 Hz, 1H), 2.44 (d, J=12.0 Hz, 1H), 1.91–1.76 (m, 1H), 1.51–1.35 (m, 1H), 1.34–1.17 (m, 2H), 0.90 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 136.1, 133.6, 77.6, 72.3, 72.2, 63.7, 56.2, 53.1, 52.0, 45.0, 44.9, 25.9, 20.8, 18.8, 18.1, −5.5, −5.6; HRMS (ESI) calcd for $C_{20}H_{35}NNaO_4Si^+$ $[M+Na]^+$ 404.2233, found 404.2228.

4.14. Preparation of aziridine 19 with PIDA

To a solution of **18** (865 mg, 2.2 mmol) in DCE (180 mL) were added silica gel (1.7 g), K_2CO_3 (608 mg, 4.4 mmol), and PIDA (870 mg, 2.7 mmol). The mixture was stirred at rt for 30 min, and heated to 50 °C for 1 h. Then directly filtered and wash with $CHCl_3$/MeOH (5:1). The filtrate was concentrated in vacuo to give a residue, which was purified by silica gel chromatography with PE/EtOAc (1:1) to yield aziridine **19** (600 mg, 70%).

4.15. Preparation of methyl quaternary ammonium salt of 19

To a solution of **19** (38 mg, 0.1 mmol) in CH_2Cl_2 (1 mL) was added CH_3I (31 μL, 0.5 mmol). After being stirred at rt for 30 min, the reaction mixture was concentrated in vacuo to get nearly pure methyl quaternary ammonium salt of **19** (52 mg, 100%). Further purification was completed through flash silica gel chromatography with $CHCl_3/CH_3OH$ (5:1) or by recrystallization. Data for methyl quaternary ammonium salt of **19**: white solid; mp: 173–175 °C; IR (KBr) ν_{max}: 2931, 2860, 1724, 1632, 1463, 1253, 1101 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.30 (d, J=4.7 Hz, 1H), 4.23 (s, 1H), 4.18 (d, J=4.7 Hz, 1H), 3.88 (d, J=13.2 Hz, 1H), 3.81 (s, 3H), 3.56 (d, J=10.0 Hz, 1H), 3.47 (s, 3H), 3.39 (d, J=10.0 Hz, 1H), 3.30 (s, 3H), 3.24 (d, J=13.2 Hz, 1H), 2.75 (d, J=15.2 Hz, 1H), 2.50 (d, J=5.2 Hz, 1H), 2.26–2.13 (m, 2H), 1.79 (t, J=14.7 Hz, 1H), 1.65–1.52 (m, 1H), 1.43 (d, J=13.6 Hz, 1H), 0.89 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 76.0, 68.3, 56.9, 56.7, 56.3, 54.6, 53.1, 50.1, 49.3, 36.3, 30.4, 27.2, 26.1, 25.8, 20.7, 18.1, −5.4, −5.6; HRMS (ESI) calcd for $C_{21}H_{38}NO_4Si^+$ $[M-I]^+$ 396.2570, found 396.2289. Crystal data: $C_{21}H_{40}INO_5Si$, M=541.53, monoclinic, a=7.2844(2) Å, b=33.8783(9) Å, c=10.5399(2) Å, β=97.380(2)°, V=2579.52(12) Å^3, T=135.00(10), space group $P2_1/c$, Z=4, μ(Mo Kα)=1.316, 10,405 reflections measured with 2.8070≤θ≤28.9366° scan, 4561 unique (R_{int}=0.0335), which were used in all calculations. The final wR_2 was 0.0901 (all data) and R_1 was 0.0385 (>2σ(I)). CCDC reference number: CCDC 927430.

4.16. Preparation of inseparable 21a and 21b

To a solution of **19** (40 mg, 0.10 mmol) in CH_2Cl_2 (1 mL) at 0 °C was added Ac_2O (20 μL, 0.21 mmol). The mixture was stirred for 1 h, then quenched with std $NaHCO_3$ solution and extracted with EtOAc. The combined organics were dried over $MgSO_4$ and concentrated to give a residue, which was purified by silica gel chromatography with PE/EtOAc (8:1) to yield an inseparable mixture of **21a** and **21b** (45 mg, 95%). For the mixture: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.40 (s, 1H), 4.79–4.65 (m, 2H), 4.44 (s, 1H), 4.13–4.03 (m, 2H), 3.89–3.78 (m, 1H), 3.74 (s, 6H), 3.70 (s, 1H), 3.47 (d, J=9.8 Hz, 1H), 3.42–3.28 (m, 6H), 3.25 (s, 3H), 3.23 (s, 3H), 2.92 (d, J=13.4 Hz, 1H), 2.71 (d, J=6.8 Hz, 1H), 2.57 (t, J=7.7 Hz, 1H), 2.50–2.29 (m, 4H), 2.20 (s, 3H), 2.10 (s, 3H), 2.00 (s, 3H), 1.96 (s, 3H), 1.92–1.82 (m, 2H), 1.80–1.46 (m, 6H), 0.89 (s, 18H), 0.03 (s, 12H).

4.17. Preparation of tricyclic amine 22a and 22b

To a solution of **19** (438 mg, 1.15 mmol) in DMF (6 mL) was added iodoethane (0.18 mL, 2.3 mmol). The mixture was stirred at 30 °C for 1 h, then NaOAc (470 mg, 5.75 mmol) was added and stirring was continued for another 5 h. The mixture was poured into 100 mL EtOAc and washed with brine (3×20 mL). The organics were dried over $MgSO_4$ and concentrated to give a residue, which was purified by silica gel chromatography with PE/EtOAc (15:1–5:1) to yield **22a** (415 mg, 77%) and **22b** (108 mg, 20%). Data for **22a**: white solid; mp: 140–142 °C; IR (KBr) ν_{max}: 2924, 2851, 1741, 1464, 1373, 1243, 1083 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.96–4.78 (m, 1H), 3.76–3.70 (m, 1H), 3.69 (s, 3H), 3.41 (d, J=14.1 Hz, 1H), 3.31 (d, J=9.7 Hz, 1H), 3.25 (d, J=9.7 Hz, 1H), 3.24 (s, 3H), 2.67–2.32 (m, 5H), 2.20–2.08 (m, 1H), 1.94 (s, 3H), 1.93–1.76 (m, 3H), 1.58–1.49 (m, 2H), 1.04 (t, J=7.1 Hz, 3H), 0.87 (s, 9H), 0.00 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 170.4, 79.9, 78.5, 71.6, 69.2, 68.6, 56.9, 53.2, 51.3, 48.7, 39.2, 37.3, 31.5, 28.6, 25.9, 24.0, 21.2, 18.3, 13.2, −5.5; HRMS (ESI) calcd for $C_{24}H_{44}NO_6Si^+$ $[M+H]^+$ 470.2938, found 470.2940. Crystal data: $C_{24}H_{43}NO_6Si$, M=469.68, monoclinic, a=7.8927(3) Å, b=28.7461(14) Å, c=12.5666(8) Å, β=106.681(6)°, V=2731.2(2) Å^3, T=293.15, space group $P2_1/n$, Z=4, μ(Mo Kα)=0.121, 11,894 reflections measured with 2.8239≤θ≤29.1888° scan, 5575 unique (R_{int}=0.0250), which were used in all calculations. The final wR_2 was 0.2042 (all data) and R_1 was 0.0736 (>2σ(I)). CCDC reference number: CCDC 927431.

Data for **22b**: white solid; mp: 86–88 °C; IR (KBr) ν_{max}: 2936, 2890, 1722, 1532, 1355 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.02 (s, 1H), 3.91 (s, 1H), 3.67 (s, 3H), 3.49 (d, J=9.3 Hz, 1H), 3.30 (d, J=9.3 Hz, 1H), 3.20 (s, 3H), 2.84 (d, J=3.4 Hz, 1H), 2.66 (d, J=11.9 Hz, 1H), 2.57–2.37 (m, 3H), 2.14 (d, J=11.9 Hz, 1H), 2.07 (d, J=15.7 Hz, 1H), 1.99 (s, 3H), 1.93 (d, J=12.5 Hz, 1H), 1.86–1.74 (m, 2H), 1.50 (d, J=13.7 Hz, 1H), 1.33–1.27 (m, 1H), 1.02 (t, J=7.1 Hz, 3H), 0.88 (s, 9H), 0.03 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 169.9, 79.6, 78.4, 71.6, 64.6, 61.7, 56.3, 53.6, 51.4, 51.0, 39.4, 38.3, 30.8, 26.9, 25.9, 21.1, 19.7, 18.2, 12.5, −5.5, −5.5; HRMS (ESI) calcd for $C_{24}H_{44}NO_6Si^+$ $[M+H]^+$ 470.2938, found 470.2940.

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Supplementary data

^{1}H and ^{13}C NMR spectra for all new compounds and NOEDS for compound **14**. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.04.102.

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41. The multiplicity of the signal of proton on the carbon attached the acetoxyl group can be used to differentiate the two isomers, since the signal of the proton at C-17 of **21b** appears as a broadened singlet at δ=5.40 ppm due to the dihedral angle between H-7 and H-17 is ca. 90° based on observation of molecular model of **21b**, while the corresponding proton signal of **21a** shows as a multiplet at δ=4.72 ppm.