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SYNTHETIC STUDIES ON PYRROLOINDOLIZIDINE SKELETON BASED ON GOLD–CATALYZED HYDROAMINATION–ENAMINE CYCLIZATION–RING–CLOSING METATHESIS STRATEGY

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*This paper is dedicated to Professor Tohru Fukuyama on the occasion of his 70*th *birthday.*

Abstract – A pyrroloindolizidine skeleton, which is observed in myrmicarin alkaloids isolated from African ant, is highly unique, oligocyclic indolizidine derivative. We describe here an attempt on a synthesis of a pyrroloindolizidine skeleton with our originally developed gold–catalyzed cascade reaction and a newly developed synthetic route for the skeleton via gold–catalyzed hydroamination–enamine cyclization–ring–closing metathesis.

INTRODUCTION

A pyrroloindolizidine skeleton is a highly unique, oligocyclic indolizidine derivative. As a natural component, it was firstly observed as a core, characteristic penta–substituted pyrrole with distinctive substituents in myrmicarin alkaloids myrmicarin 215A, 215B, and 217 (Figure 1).[1] They were isolated from African ant, *Myrmicaria opaciventris*, as the biologically active constituents of the poison gland

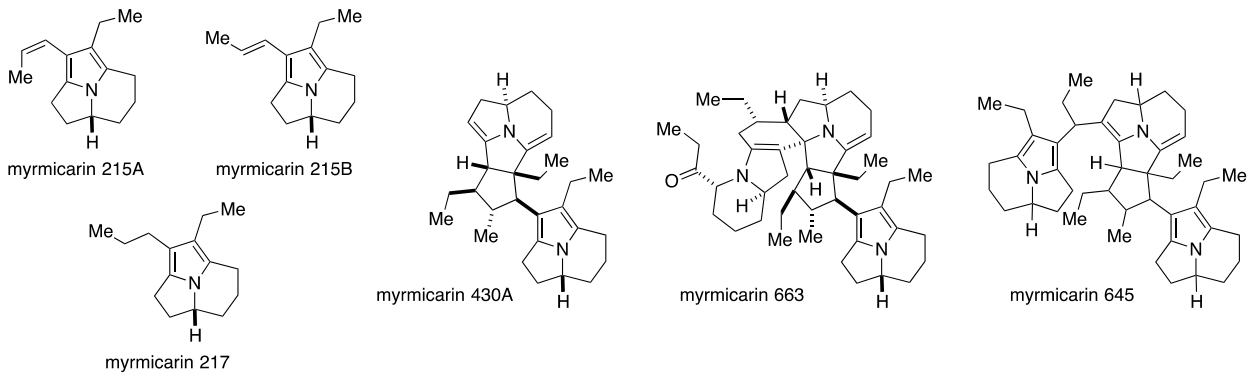
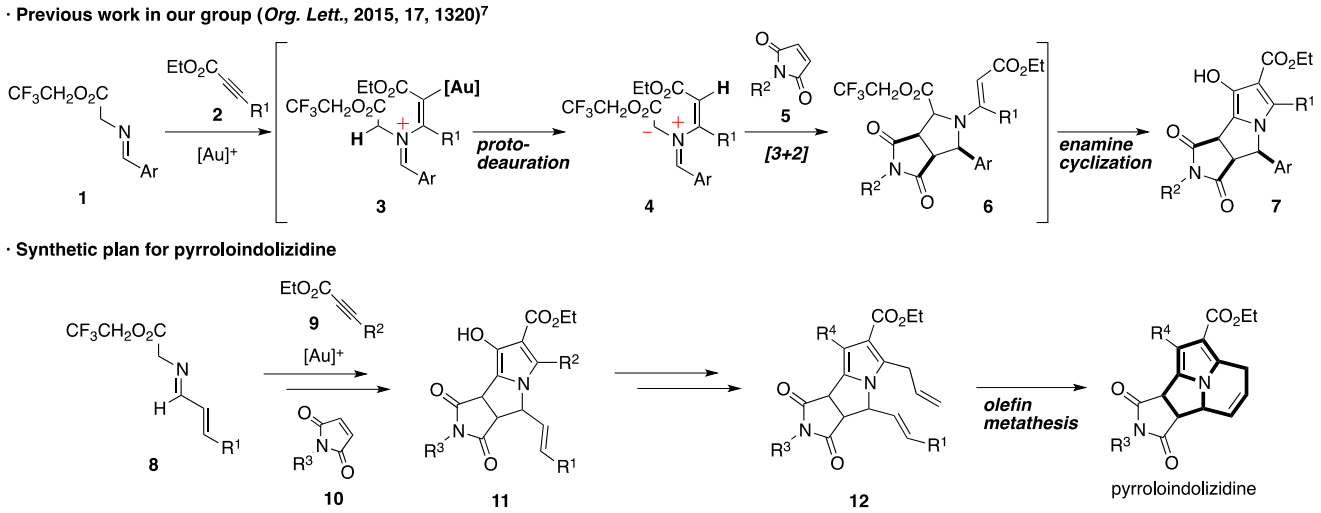


Figure 1. Natural pyrroloindolizidines, myrmicarins

secretion and higher–ordered components myrmicarins 430A, 663, and 645 were also detected through the extensive studies.[2] From their potency as a medicine, a structural feature, and a sensitivity to air, silica gel, and alumina, a series of these alkaloids have been paid huge attentions of synthetic organic chemists. Especially, myrmicarin 215A and B, which are suggested as the precursor for higher–ordered derivatives, were focused as suitable synthetic targets for comprehensive total syntheses of these alkaloids. In 2005, five years later from the first enantioselective total synthesis of (+)–(*R*)–myrmicarin 217 by Vallée and co–workers,[3] Movassaghi and co–worker established the collective synthesis of myrmicarin 215A, B, and 217 via a catalytic asymmetric reduction of enoate.[4] Furthermore, synthetic studies on dimeric 430A from 215B were reported.[5] Snyder and co–workers also completed syntheses of 215A and B then through a dimerization reaction of their precursor dienamine, a total synthesis of 430A was attempted.[6] However, they only arrived at unnatural isomers. Thus, novel variable synthetic routes for the core pyrroloindolizidine skeleton are still anticipated.

Recently, we developed a novel three–component approach to pyrrolizidines via gold–catalyzed azomethine ylide formation followed by enamine cyclization reaction (Scheme 1).[7] Trifluoroethyl arylidene glycinate **1** could react with the propiolate activated by a gold catalyst to give vinylgold **3** and subsequent protodeauration afforded azomethine ylide **4**. After the cycloaddition of **4** with maleimide **5**, resultant unstable enamine **6** was transformed into pyrrolizidine **7**, a distinctively penta–substituted pyrrole, via cyclization–aromatization sequence. As an application of this reaction, we planned a novel synthetic route for pyrroloindolizidines with advanced substrates, α,β–unsaturated aldimine **8** and functionalized propiolate **9**. After appropriate functional group manipulation, resultant penta–substituted pyrrole **11** would be lead to the pyrroloindolizidine skeleton through a ring–closing metathesis of diene **12**. In this manuscript, our attempt on a synthesis of a pyrroloindolizidine skeleton along this line and a newly established route via hydroamination–enamine cyclization–olefin metathesis are described.

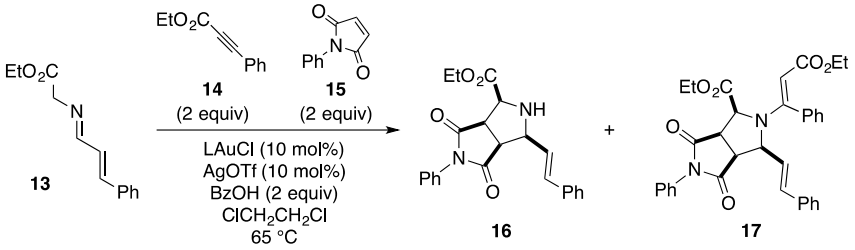


Scheme 1. Blueprint for a construction of a pyrroloindolizidine skeleton

RESULTS AND DISCUSSION

As extended studies of our previous work, we examined the gold–catalyzed azomethine ylide formation from iminoester **13** under the optimal conditions for benzylidene iminoester (Table 1, entries 1 and 2).[7] However, the desired enamine **17** could not been obtained at all. Instead of **17**, we detected small amount of pyrrolidine **16**[8] through a cycloaddition of the azomethine ylide generated from 1,2–proton migration of **13** followed by cycloaddition with **15**. When the gold catalyst possessing Buchwald ligand was applied for the reaction (entries 3 and 4), enamine **17** could be formed in low yield.[9] The TLC analysis of the reaction suggested that the desired enamine **17** was produced by a hydroamination reaction of the pyrrolidine **16**. The lowered nucleophilicity of **13** by the conjugation compared with the benzylidene iminoester **1** would be a reason why the azomethine ylide formation from **13** itself proceeded prior to the desired nucleophilic attack of **13** to the activated **14**.[10] Further survey neither of alternative substrates, gold catalysts, nor under higher reaction temperature did work well. Furthermore, the iminoester derived from aliphatic aldehydes, which can be transformed in to alkene functionality, had been suggested to be unacceptable in our previous three–component coupling. Thus, we revised the synthetic route to start from a hydroamination reaction of pyrrolidine. Although several hydroamination reaction between pyrrolidines and electron–deficient alkynes are reported,[11] gold–catalyzed condition which enables highly selective activation of alkynes would be suitable to preserve the pendant labile trifluoroethyl ester, an essential functionality for subsequent enamine cyclization.

Table 1. Attempt on the Au–catalyzed azomethine ylide formation

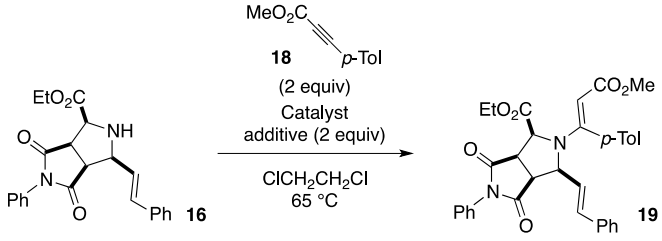


Entry	Gold Catalyst	Time (h)	Yield (%)	
			16	**17**
1	$(Ph_3P)AuCl$	2	12	–
2	$(Ph_3P)AuCl$	4	7	–
3	CyJohnPhosAuCl	4	–	13%
4	XPhosAuCl	4	–	14%

As shown in Table 2, we newly optimized the conditions for hydroamination reaction of easily accessible **16** with propiolate **18**. We confirmed that the process leading to **19** was actually catalyzed by a gold complex (entry 1) and Buchwald ligands, especially highly bulky *t*–BuXPhos (entry 6), were effective for

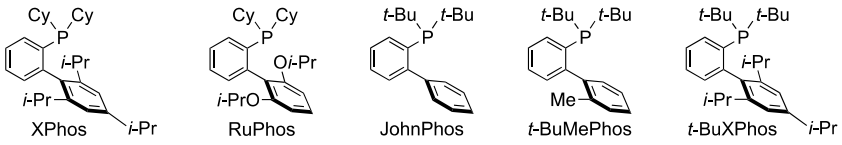
the transformation (entries 2–6). Among the several counter anions, $^{-}NTf_2$ afforded **19** in slightly higher yield (entry 10) and fortunately bench–stable *t*–BuXPhosAuNTf$_2$ was most effective (entry 11). Finally, we found that the acid, which accelerated a protodeauration reaction of the enamine–gold complex,[7] is not necessary for the enhancement of the catalytic turn–over (entries 12–14). In this case, we reasoned that electron–rich *t*–BuXPhos would increase the electronic density of the gold metal and enhance the reactivity of vinyl gold complex toward a proton.[12]

Table 2. Au–Catalyzed hydroamination reaction of pyrrolidine and propiolate



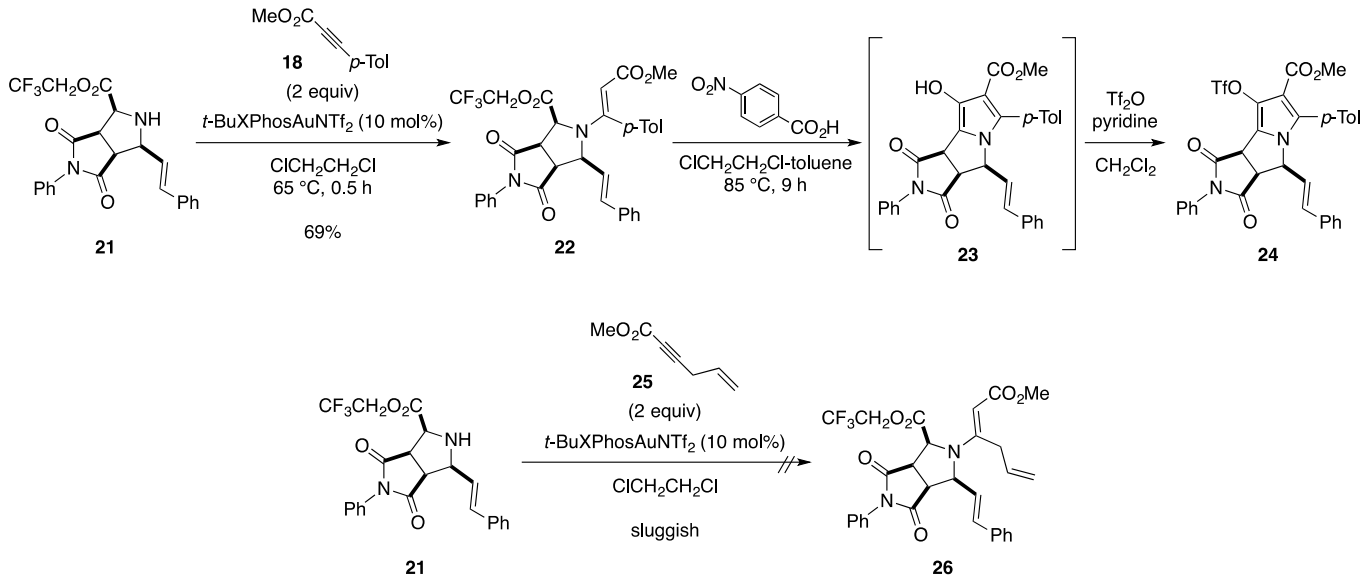
Entry	Catalyst	Additive	Time (h)	Yield (%)
1	none	BzOH	2	–
2	XPhosAuCl (10 mol%), AgOTf (10 mol%)	BzOH	0.5	46
3	RuPhosAuCl (10 mol%), AgOTf (10 mol%)	BzOH	0.5	68
4	JohnPhosAuCl (10 mol%), AgOTf (10 mol%)	BzOH	0.5	77
5	*t*-BuMePhosAuCl (10 mol%), AgOTf (10 mol%)	BzOH	0.5	70
6	*t*-BuXPhosAuCl (10 mol%), AgOTf (10 mol%)	BzOH	0.5	80
7	*t*-BuXPhosAuCl (10 mol%), $AgBF_4$ (10 mol%)	BzOH	0.5	58
8	*t*-BuXPhosAuCl (10 mol%), $AgPF_6$ (10 mol%)	BzOH	0.5	76
9	*t*-BuXPhosAuCl (10 mol%), $AgSbF_6$ (10 mol%)	BzOH	1.5	41
10	*t*-BuXPhosAuCl (10 mol%), $AgNTf_2$ (10 mol%)	BzOH	0.5	64 (79)[a]
11	*t*-BuXPhosAuNTf$_2$ (10 mol%)	BzOH	0.5	82
12	*t*-BuXPhosAuNTf$_2$ (10 mol%)	CSA	2	– (78% recovery)
13	*t*-BuXPhosAuNTf$_2$ (10 mol%)	EtOH	0.5	81
14	*t*-BuXPhosAuNTf$_2$ (10 mol%)	none	0.5	94

[a]Yield in parentheses is the yield based on recovered starting material.

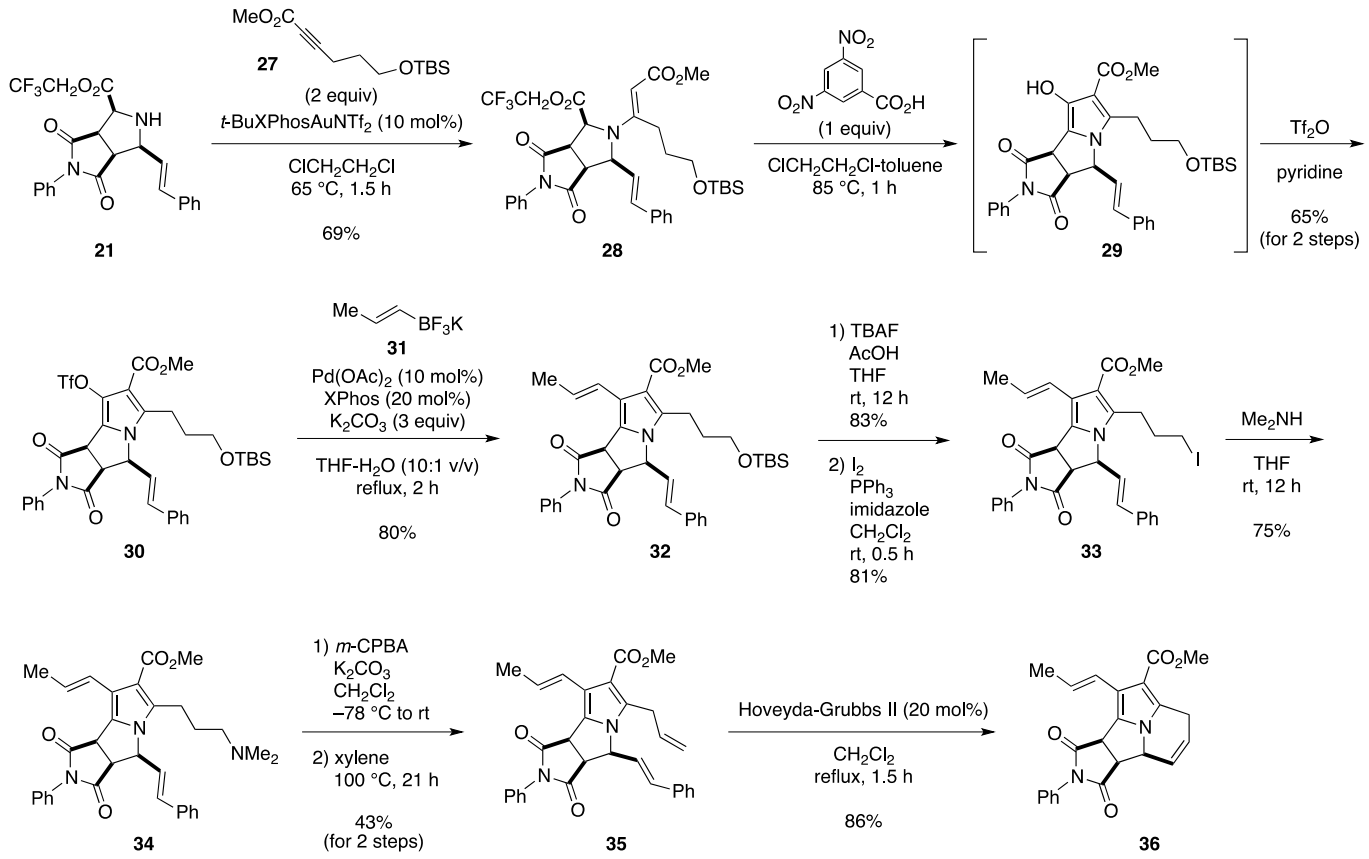


We then investigated the conditions for the enamine cyclization step with the enamine **22** (Scheme 2). Appropriate pyrrolidine **21**, which was equipped with trifluoroethyl ester group, was uneventfully reacted with **18** to yield the precursor enamine **22**. Compared with our previous report,[7] a slightly acidic activator was required and the pyrrole **24** could be obtained after triflation of resultant hydroxypyrrole **23**. Because of the air–sensitivity of **23**, it should be noted that the triflation reaction of **23** had to be conducted after work–up as soon as possible. With the best handling of these intermediates, however, the advanced enamine **26**, which could realize the conceivably shortest synthetic route for pyrroloindolizidines, could

not be prepared because of the instability of **25** (skipped enyne) or **26** (skipped diene) under the reaction conditions.



Scheme 2. Trial of pyrrole formation reaction with trifluoroethyl ester



Scheme 3. Synthesis of a pyrroloindolizidine skeleton

In this context, we decided to set up the olefin on the metathesis precursor via an elimination reaction. The enamine **28** was prepared by the gold–catalyzed hydroamination reaction between **21** and **27** in good

yield. The enamine cyclization of **28** to the penta–substituted pyrrole **29** required more acidic activator 3,5–dinitrobenzoic acid than that for **22**, and subsequent triflation afforded the triflate **30** in 65% for 2 steps. The propenyl group could be installed by modified Suzuki–Miyaura coupling reaction[13] in the presence of $Pd(OAc)_2$, XPhos, and K_2CO_3. After desilylation of **32**, we applied a Grieco–Nishizawa method on the resultant primary alcohol; however, the desired olefin didn't observed at all. Furthermore, elimination reactions of **33** in basic condition didn't give the metathesis precursor **35**. Thus, we employed a Cope elimination of tertiary amine **34** to afford the requisite diene **35**, of which ring–closing metathesis finally established a desired pyrroloindolizidine core in high yield.

In summary, we accomplished a novel synthetic pathway for a pyrroloindolizidine skeleton based on a gold–catalyzed hydroamination–enamine cyclization–ring–closing metathesis strategy. This strategy involves an intermolecular convergent approach, which would enable an easy setup for the entirely and distinctively substituted pyrrole core in the myrmicarins. Since the removal of pyrrolidinedione moiety derived from dipolarophile maleimide via reductive manipulation of the imide functionality faced on difficulties, studies on collective synthesis of myrmicarin alkaloids starting with corresponding monocyclic congener are ongoing in our laboratory.

EXPERIMENTAL

All nonaqueous reactions were carried out under an Ar atmosphere. Reagents were purchased from commercial suppliers and used as received. Anhydrous solvents were prepared by distillation over CaH_2, or purchased from commercial suppliers. ^1H and ^{13}C NMR spectra were measured on a JEOL ECA 500 II, ECX 400, or a Varian GEMINI 300 instrument using tetramethylsilane (0.00 ppm for ^1H in $CDCl_3$), $CHCl_3$ (7.26 ppm for ^1H in $CDCl_3$), $CDCl_3$ (77.0 ppm, triplet for ^{13}C in $CDCl_3$), and benzene (7.15 ppm for ^1H and 128.00 ppm, triplet for ^{13}C in benzene–d_6) as an internal reference. The following abbreviations are used for spin multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, ddd = double of doublet of doublets, dq = doublet of quartets, tt = triplet of triplets, m = multiplet, and br = broad. *J* values were in hertz. Mass spectra were measured on JEOL JMS–GCmate II or a JEOL JMS–AX 505 HAD mass spectrometer. IR spectra were recorded on a JASCO FT/IR–460Plus spectrometer. Column chromatography was carried out by employing Cica Silica Gel 60N (spherical, neutral, 40–50 μm). Thin layer chromatography was performed on precoated silica gel 60 F_{254} plates (Merck).

Iminoester 13. To a suspension of ethyl glycinate hydrochloride (115 mg, 0.596 mmol) in CH_2Cl_2 (1.32 mL) were added Et_3N (83.3 μL, 0.596 mmol) and $MgSO_4$ (224 mg) at room temperature. After the mixture was stirred at this temperature for 30 min, *trans*–cinnamaldehyde (50 μL, 0.397 mmol) was added to the mixture at room temperature. The reaction mixture was stirred for 3 h at room temperature

until completion of the reaction (monitored with ^{1}H NMR). After filtration, the organic phase was washed with sat. aq. NH_4Cl, dried over $MgSO_4$, filtered, and concentrated in *vacuo*. The resultant crude iminoester **13** (97.3 mg, quant.) was conducted to the gold catalyzed reaction without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (1H, s), 7.50–7.34 (5H, m), 7.10–6.99 (2H, m), 4.32 (2H, s), 4.25 (2H, q, J = 7.1 Hz), 1.31 (3H, t, J = 7.1 Hz).

General procedure for Table 1. To a solution of iminoester (0.100 mmol) in $ClCH_2CH_2Cl$ (0.10 mL) was added ethyl phenylpropiolate (0.200 mmol), *N*–phenylmaleimide (0.200 mmol), LAuCl (0.0100 mmol), AgOTf (0.0100 mmol) and BzOH (0.200 mmol) at room temperature. After stirred at 65 °C for several hours, the reaction was quenched with sat. aqueous $NaHCO_3$. The aqueous phase was extracted with CH_2Cl_2, and the combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated in *vacuo*. The residue was purified by flash column chromatography on silica gel (eluent: hexane/AcOEt = 60:40 ~ 50:50) to afford the product.

Pyrrolidine 16.[8] Colorless solid, mp 172–175 °C (lit[8] mp 162–170 °C); R_f = 0.36 (hexane/AcOEt = 40:60); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46–7.22 (10H, m), 6.75 (1H, d, J= 15.9 Hz), 6.43 (1H, dd, J= 15.9, 6.9 Hz), 4.32 (2H, q, J= 7.1 Hz), 4.13 (2H, dd, J= 8.8, 7.7 Hz), 3.73 (1H, dd, J= 8.0, 7.4 Hz), 3.54 (1H, dd, J= 8.0, 7.7 Hz), 2.36 (1H, br s), 1.35 (3H, t, J= 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 174.1, 169.7, 136.3, 132.7, 131.6, 129.1, 128.7, 128.5, 127.9, 126.7, 126.4, 125.0, 62.9, 62.9, 61.8, 49.6, 48.9, 14.1; IR (KBr) 1720 cm^{-1}; MS (EI) *m/z* 390 $(M)^+$; HRMS (EI) calcd for $C_{23}H_{22}N_2O_4$ $(M)^+$ 390.1580, found 390.1574.

Enamine 17. Colorless solid, mp 99–105 °C; R_f = 0.43 (hexane/AcOEt = 40:60); ^{1}H NMR (400 MHz, benzene–d_6) δ 7.22–7.10 (9H, m), 6.99–6.96 (6H, m), 6.65 (1H, dd, J = 16.4, 8.4 Hz), 6.46 (1H, d, J= 16.4 Hz), 5.32 (1H, s), 4.57 (1H, dd, J = 8.8, 8.4 Hz), 4.47 (1H, d, J= 9.2 Hz), 4.28–4.04 (2H, m), 3.98–3.88 (2H, m), 3.08–2.99 (2H m), 0.97 (3H, t, J= 6.8 Hz), 0.85 (3H, t, J= 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.5, 172.4, 170.1, 166.9, 158.1, 135.8, 135.2, 135.1, 131.0, 129.1, 128.9, 128.7, 128.6, 128.5, 128.2, 128.1, 126.8, 126.3, 123.5, 91.8, 64.0, 62.5, 62.1, 58.8, 49.6, 47.3, 14.2, 14.0; IR (KBr) 1735, 1709 cm^{-1}; MS (EI) *m/z* 564 $(M)^+$; HRMS (EI) calcd for $C_{34}H_{32}N_2O_6$ $(M)^+$ 564.2260, found 564.2221.

Trimethyl(2–*p*–tolylethynyl)silane (S1).[14] To a stirred solution of 4–iodotoluene (5.45 g, 25.0 mmol) in DMF (41 mL) were added trimethylsilylacetylene (2.70 g, 27.5 mmol), $Pd(PPh_3)_2Cl_2$ (246 mg, 0.350 mmol), CuI (285 mg, 1.50 mmol), and Et_3N (9.13 g, 90.0 mmol) at room temperature. After stirred for 3 h at 50 °C, the reaction was quenched with water. The aqueous phase was extracted with Et_2O and the combined organic phases were washed with sat. aqueous NH_4Cl and brine, dried over $MgSO_4$, filtered, and concentrated in *vacuo*. The residue was purified by flash column chromatography on silica gel (eluent: hexane) to afford the acetylene **S1** (4.66 g, 98%) as a colorless oil.

R_f = 0.55 (hexane only)

^{1}H NMR spectrum of the acetylene **S1** was identical with that previously reported.[14]

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36(2H, d, *J* = 6.3 Hz), 7.10 (2H, d, *J* = 6.9 Hz), 2.34 (3H, s), 0.25 (9H, s).

Methyl *p*–methylphenylpropiolate (18). The ester was prepared according to the procedure reported by Yamamoto and co–workers.[15] In a round bottomed two–necked flask, CsF (884 mg, 5.83 mg) was dried in vacuo at 120 °C for 1 h. The flask was filled with CO_2 gas (balloon) and DMF (1.5 mL). To the above suspension was added dropwise the solution of **S1** (550 mg, 2.93 mmol) in DMF (5.9 mL) at room temperature. After stirred for 6 h at room temperature, methyl iodide (497 mg, 3.21 mmol) was added to the reaction mixture. After stirred for 12 h at room temperature, the reaction was quenched with sat. aqueous NH_4Cl and aqueous phase was extracted with AcOEt. The combined organic phases were washed with water and brine, dried over $MgSO_4$, filtered, and concentrated in *vacuo*. The residue was purified by flash column chromatography on silica gel (eluent: hexane/AcOEt = 95:5) to afford the propiolate **18** (390 mg, 77%) as a yellow solid.

R_f = 0.52 (hexane only)

^{1}H NMR spectrum of the propiolate **18** was identical with that previously reported.[15]

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (2H, d, *J* = 8.1 Hz), 7.18 (2H, d, *J* = 8.4 Hz), 3.83 (3H, s), 2.38 (3H, s).

Preparation of pyrrolidine 16. The pyrrolidine **16** was prepared according to the procedure reported by Shi, Gan and co–workers.[16] To a suspension of ethyl glycinate hydrochloride (1.35 g, 9.71 mmol) in CH_2Cl_2 (22.0 mL) were added Et_3N (0.978 g, 9.71 mmol) and $MgSO_4$ (3.65 g) at room temperature. After the mixture was stirred at this temperature for 20 min, *trans*–cinnamaldehyde (1.29 g, 9.71 mmol) and silica gel (1.35 g) were added to the mixture at 0 °C. After stirred at 0 °C for 3 h, the mixture was filtered and diluted with CH_2Cl_2 (15 mL). To the above solution was added *N*–phenylmaleimide (1.68 g, 9.71 mmol) and AgOAc (48.4 mg, 0.290 mmol) at room temperature. After stirred for 12 h in a dark, the suspension was filtered through a Celite pad and the filtrate was concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (eluent: hexane/AcOEt = 95:5) to afford the pyrrolidine **16** (1.08 g, 35%).

General procedure for enamine synthesis (Entry 13 in Table 2). To a stirred solution of **16** (39.7 mg, 0.102 mmol) in $ClCH_2CH_2Cl$ (0.10 mL) were added propiolate **18** (35.4 mg, 0.205 mmol) and *t*–BuXPhosAuNTf$_2$ (9.2 mg, 0.0102 mmol) at room temperature. After stirred for 0.5 h at 65 °C, the reaction was quenched with sat. aqueous $NaHCO_3$ and the aqueous phase was extracted with CH_2Cl_2. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated in *vacuo*. The residue was purified by flash column chromatography on silica gel (eluent: hexane/AcOEt = 50:50) to afford the enamine **19** (54.0 mg, 94%) as a colorless solid.

R_f = 0.35 (hexane/AcOEt = 50:50); mp 189–191 °C (decomp.); ^{1}H NMR (400 MHz, benzene–d_6) δ 7.22–7.12 (5H, m), 6.99–6.85 (9H, m), 6.65 (1H, dd, J = 16.0, 7.6 Hz), 6.50 (1H, d, J = 16.0 Hz), 5.32 (1H, s), 4.62 (1H, dd, J = 16.0, 9.6 Hz), 4.51 (1H, d, J = 9.6 Hz), 4.07–4.03 (2H, m), 3.34 (3H, s), 3.14–3.05 (2H, m), 2.10 (3H, s), 0.97 (3H, t, J = 6.8 Hz); ^{13}C NMR (100 MHz, benzene–d_6) δ 173.5, 172.0, 176.4, 166.8, 158.7, 138.3, 136.3, 135.1, 132.8, 132.1, 129.2, 129.0, 128.9, 128.8, 128.3, 127.1, 126.7, 124.6, 92.0, 64.4, 63.0, 62.1, 50.0, 49.7, 47.4, 21.3, 13.9; IR (KBr) 1738, 1721, 1698, 1578, 1160, 1140 cm^{-1}; MS (EI) *m/z* 564 (M^+); HRMS (EI) *m/z* calcd for $C_{34}H_{33}N_2O_6$ (M^+) 564.2260, found: 564.2259.

Pyrrolidine 21. According to the same procedure described for the synthesis of pyrrolidine **16**, the pyrrolidine **21** (718 mg, 48%, colorless solid) was obtained from trifluoroethyl glycine hydrochloride[7] (652 mg, 3.37 mmol).

R_f = 0.51 (hexane/AcOEt = 50:50); mp 138–141 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45–7.36 (7H, m), 7.32–7.29 (3H, m), 6.76 (1H, d, J = 16.0 Hz), 6.37 (1H, d, J = 16.0, 7.0 Hz), 4.78 (1H, dq, J = 12.5, 8.0 Hz), 4.45 (1H, dq, J = 12.5, 8.0 Hz), 4.23 (1H, d, J = 7.0 Hz), 4.17 (1H, dd, J = 7.5, 7.0 Hz), 3.79 (1H, dd, J = 7.5, 7.0 Hz), 3.54 (1H, t, J = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.9, 173.8, 168.5, 136.2, 133.0, 131.5, 129.2, 128.8, 128.6, 128.0, 126.8, 126.3, 124.9, 122.9 (q, J = 274 Hz), 62.5, 61.8, 61.3 (q, J = 37.2 Hz), 48.8, 48.6; IR (KBr) 3333, 1770, 1711, 1179 cm^{-1}; MS (EI) *m/z* 444 (M^+); HRMS (FAB) *m/z* calcd for $C_{23}H_{19}F_3N_2O_4$ (M^+) 444.1297, found: 444.1252.

Enamine 22. According to the same procedure described for the synthesis of enamine **19**, the enamine (95.2 mg, 69%, colorless solid) was obtained from pyrrolidine **21** (100 mg, 0.255 mmol).

R_f = 0.36 (hexane/AcOEt = 60:40, three times); mp 204–205 °C (decomp.); ^{1}H NMR (400 MHz, benzene–d_6) δ 7.22–7.19 (2H, m), 7.15–7.07 (4H, m), 6.98–6.96 (5H, m), 6.91–6.81 (3H, m), 6.66 (1H, d, J = 16.0 Hz), 6.39 (1H, d, J = 16.0, 8.4 Hz), 5.26 (1H, s), 4.54 (1H, dd, J = 8.4, 8.4 Hz), 4.40 (1H, d, J = 9.6 Hz), 4.20–4.02 (2H, m), 3.33 (3H, s), 2.94 (1H, dd, J = 9.2, 9.2 Hz), 2.86 (1H, dd, J = 9.6, 9.2 Hz), 2.10 (3H, s); ^{13}C NMR (100 MHz, benzene–d_6) δ 173.3, 171.5, 169.4, 166.5, 158.1, 138.7, 136.0, 135.5, 132.4, 131.7, 129.02, 128.9, 128.8, 128.6, 128.3, 128.2, 128.1, 127.8, 127.1, 126.5, 123.7, 92.8, 64.2, 62.0, 61.8 (q, J = 36.5 Hz), 50.0, 49.7, 47.1, 21.1 (two signals overlapping with solvent peaks could not be detected); IR (KBr) 1764, 1719, 1697, 1578, 1161, 1141 cm^{-1}; MS (EI) *m/z* 618 (M^+); HRMS (EI) *m/z* calcd for $C_{34}H_{29}F_3N_2O_6$ (M^+) 618.1978, found 618.2009.

Triflate 24. To a solution of the enamine **22** (31.5 mg, 0.0517 mmol) in $ClCH_2CH_2Cl$–toluene (0.2 mL, 1:1 v/v) was added *p*–nitrobenzoic acid (8.60 mg, 0.0517 mmol) at room temperature. After stirred for 9 h at 85 °C, the reaction was quenched with sat. aqueous $NaHCO_3$ and the aqueous phase was extracted with CH_2Cl_2. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and concentrated in *vacuo*. To the stirred solution of the residue in CH_2Cl_2 (0.23 mL) were added pyridine (10.8 mg, 0.137 mmol) and Tf_2O (38.7 mg, 0.137 mmol) at 0 °C. After stirred for 2 h at room temperature,

the reaction was quenched with water and the aqueous phase was extracted with CH_2Cl_2. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and concentrated in *vacuo*. The residue was purified by flash column chromatography on silica gel (eluent: hexane/AcOEt = 70:30) to afford the triflate **24** (22.1 mg, 68% for 2 steps) as a red solid.

R_f = 0.28 (hexane/AcOEt = 70:30); mp 103–106 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33–7.21 (3H, m), 7.17 (2H, d, *J* = 8.0 Hz), 7.10–7.02 (4H, m), 7.02–7.00 (2H, m), 5.88 (1H, d, *J* = 16.0 Hz), 5.73 (1H, dd, *J* = 16.0, 7.5 Hz), 5.47 (1H, dd, *J* = 9.0, 7.5 Hz), 4.78 (1H, d, *J* = 9.0 Hz), 4.44 (1H, dd, *J* = 9.0, 9.0 Hz), 3.74 (3H, s), 2.26 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.1, 171.2, 162.2, 139.2, 134.9, 134.7, 134.1, 131.0, 129.6, 129.2, 128.9, 128.55, 128.52, 128.4, 126.7, 126.4, 126.3, 121.9, 121.1 (q, *J* = 320 Hz), 120.7, 110.6, 61.6, 51.9, 44.1, 21.3; IR (KBr) 1724 cm^{-1}; MS (EI) *m/z* 650 (M^+); HRMS (EI) *m/z* calcd for $C_{33}H_{25}F_3N_2O_7Si$ (M^+) 650.1335, found 650.1320.

Methyl hex–5–en–2–ynoate (25).[17] The titled compound was prepared according to the procedure reported by Hilt and co–workers.[17] To a solution of CuI (339 mg, 1.78 mmol), Na_2SO_3 (1.12 g, 8.89 mmol), and $KHCO_3$ (1.79 g, 17.8 mmol) in DMSO (17.8 mL) were added methyl propiolate (1.50 g, 17.8 mmol) and allyl bromide (2.59 g, 21.4 mmol) at room temperature. After stirred at 50 °C for 15 h, the reaction was quenched with sat. aqueous NH_4Cl and aqueous phase was extracted with Et_2O. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated in *vacuo*. The residue was purified by flash column chromatography on silica gel (eluent: pentane/Et_2O = 20:1) to afford the propiolate **25** (1.66 g, 75%) as a colorless oil.

R_f = 0.55 (hexane/AcOEt = 90:10)

^{1}H NMR spectrum of the ester was identical with that previously reported.[17]

^{1}H NMR (300 MHz, $CDCl_3$) δ□5.77 (1H, ddd, *J* = 16.8, 10.2, 5.4 Hz), 5.33 (1H, d, *J* = 16.8 Hz), 5.18 (1H, d, *J* = 10.2 Hz), 3.75 (3H, s), 3.10 (2H, d, *J* = 5.4 Hz).

***tert*–Butyldimethyl(pent–4–ynyloxy)silane (S2).**[18] To a stirred solution of 4–pentyn–1–ol (2.98 g, 35.4 mmol) in CH_2Cl_2 (45.0 mL) were added TBSCl (6.39 g, 42.6 mmol) and Et_3N (5.40 g, 53.2 mmol) at 0 °C. After stirred for 18 h at room temperature, the suspension was filtered through a Celite Pad and the filtrate was concentrated in *vacuo*. The residue was purified by flash column chromatography on silica gel (eluent: hexane/AcOEt = 98:2) to afford the silyl ether **S2** (5.60 g, 80%) as a colorless oil.

R_f = 0.55 (hexane/AcOEt = 95:5)

^{1}H NMR spectrum of the ester was identical with that previously reported.[18]

^{1}H NMR (300 MHz, $CDCl_3$) δ 3.70 (2H, t, *J* = 6.0 Hz), 2.27 (2H, t, *J* = 6.0 Hz), 1.93 (1H, s), 1.73–1.68 (2H, m), 0.90 (9H, s), 0.057 (6H, s).

Methyl 6–(*tert*–butyldimethylsilyloxy)hex–2–ynoate (27).[19] To a solution of **S2** (890 mg, 4.48 mmol) in THF (17.2 mL) was added BuLi (1.6 M in hexane, 3.6 mL, 5.82 mmol) at –78 °C. After stirred for 20 min,

methyl chloroformate (550 mg, 5.82 mmol) was added to the reaction mixture at the same temperature. After stirred for 3 h at 0 °C, the reaction was quenched with sat. aqueous NH_4Cl and aqueous phase was extracted with Et_2O. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated in *vacuo*. The residue was purified by flash column chromatography on silica gel (eluent: hexane/AcOEt = 98:2) to afford the ester **27** (1.00 g, 87%) as a colorless oil.

R_f = 0.39 (hexane/AcOEt = 95:5)

^{1}H NMR spectrum of the ester was identical with that previously reported.[19]

^{1}H NMR (300 MHz, $CDCl_3$) δ 3.75 (3H, s), 3.68 (2H, t, *J* = 6.0 Hz), 2.43 (2H, t, *J* = 6.9 Hz), 1.77 (2H, tt, *J* = 6.9, 6.0 Hz), 0.88 (9H, s), 0.046 (6H, s).

Enamine 28. According to the same procedure described for the synthesis of enamine **19**, the enamine **28** (75.9 mg, 69%, colorless solid) was obtained from pyrrolidine **21** (70.2 mg, 0.158 mmol).

R_f = 0.57 (hexane/AcOEt = 60:40); mp 166–167 °C; ^{1}H NMR (400 MHz, benzene–d_6) δ 7.27–7.26 (2H, m), 7.15–7.08 (3H, m), 6.96–6.95 (3H, m), 6.91–6.84 (3H, m), 6.49 (1H, dd, *J* = 16.0, 6.8 Hz), 4.99 (1H, dd, *J* = 8.0, 8.0 Hz), 4.83 (1H, s), 4.35 (1H, d, *J* = 9.6 Hz), 4.25–4.18 (2H, m), 3.71–3.64 (1H, m), 3.63–3.59 (1H, m), 3.52 (3H, s), 3.39–3.32 (1H, m), 2.96–2.87 (3H, m), 2.11–2.02 (1H, m), 1.89–1.79 (1H, m), 0.96 (9H, s), 0.052 (6H, d, *J* = 7.6 Hz); ^{13}C NMR (100 MHz, benzene–d_6) δ□173.2, 171.5, 168.8, 167.7, 161.4, 135.9, 135.2, 131.7, 128.9, 128.8, 128.7, 127.8, 127.1, 126.6, 125.5 (q, *J* = 225 Hz), 124.4, 89.4, 63.1, 62.9, 61.8 (q, *J* = 36.2 Hz), 61.4, 50.2, 49.5, 47.2, 32.9, 26.3, 26.2, 18.5, –5.21; IR (KBr) 1769, 1724, 1676, 1569, 1150 cm^{-1}; MS (EI) *m/z* 701 (M^++1); HRMS (FAB) *m/z* calcd for $C_{36}H_{44}F_3N_2O_7Si$ (M^++1) 701.2870, found 701.2846.

Triflate 30. To a solution of the enamine **28** (300 mg, 0.428 mmol) in $ClCH_2CH_2Cl$–toluene (1.72 mL, 1:1 v/v) was added 3,5–dinitrobenzoic acid (90.8 mg, 0.428 mmol) at room temperature. After stirred for 1 h at 85 °C, the reaction was quenched with sat. aqueous $NaHCO_3$ and the aqueous phase was extracted with CH_2Cl_2. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and concentrated in *vacuo*. The residue was diluted with pyridine (1.4 mL) and Tf_2O (235 mg, 0.856 mmol) was added to the stirred pyridine solution at 0 °C. After stirred for 1 h at room temperature, the reaction was quenched with water and the aqueous phase was extracted with CH_2Cl_2. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and concentrated in *vacuo*. The residue was purified by flash column chromatography on silica gel (eluent: hexane/AcOEt = 80:20) to afford the triflate **30** (20.4 mg, 65% for 2 steps) as a colorless solid.

R_f = 0.60 (hexane/AcOEt = 70:30); mp 76–79 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31–7.26 (8H, m), 7.02–7.00 (2H, m), 6.29–6.19 (2H, m), 5.54 (1H, dd, *J* = 9.6, 4.8 Hz), 4.68 (1H, d, *J* = 9.2 Hz), 4.43 (1H, dd, *J* = 9.6, 9.2 Hz), 3.84 (3H, s), 3.60–3.53 (2H, m), 3.05–2.98 (1H, m), 2.81–2.74 (1H, m), 1.81–1.74 (2H, m), 0.85 (9H, s), –0.01 (6H, d, *J* = 3.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 171.4, 162.7,

136.1, 134.6, 134.1, 131.0, 129.1, 128.94, 128.93, 128.7, 128.3, 126.9, 126.3, 123.0, 119.3, 118.5 (q, J = 319 Hz), 109.7, 62.3, 60.6, 52.5, 51.0, 43.8, 32.1, 25.8, 22.7, 18.2, 14.1, –5.4; IR (KBr) 1723, 1242, 1203 cm^{-1}; MS (FAB) *m/z* 733 (M^++1); HRMS (FAB) *m/z* calcd for $C_{35}H_{40}F_3N_2O_8SSi$ (M^++1) 733.2227, found 733.2225.

Pyrrole 32. To a stirred solution of the triflate **30** (32.4 mg, 0.0437 mmol) in THF–H_2O (0.16 mL, 10:1 v/v) were added potassium *trans*–1–propenyltrifluoroborate (**31**) (12.7 mg, 0.873 mmol), XPhos (4.30 mg, 0.00873 mmol), K_2CO_3 (18.3 mg, 0.131 mmol), and $Pd(OAc)_2$ (1.00 mg, 0.00437 mmol) at room temperature. After stirred for 2 h at 70 °C, the reaction was quenched with water and the aqueous phase was extracted with AcOEt. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and concentrated in *vacuo*. The residue was purified by flash column chromatography on silica gel (eluent: hexane/AcOEt = 80:20) to afford the pyrrole **32** (22.4 mg, 81%) as a red solid.

R_f = 0.59 (hexane/AcOEt = 70:30); mp 156–157 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30–7.25 (8H, m), 6.97 (2H, d, J = 7.0 Hz), 6.93 (1H, d, J = 16.0 Hz), 6.77–6.70 (1H, m), 6.32 (1H, dd, J = 16.0, 6.0 Hz), 6.23 (1H, d, J = 16.0 Hz), 5.49–5.46 (1H, m), 4.50 (1H, d, J = 9.0 Hz), 4.45 (1H, dd, J = 9.0, 9.0 Hz), 3.85 (3H, s), 3.65–3.55 (2H, m), 2.99–2.94 (1H, m), 2.80–2.74 (1H, m), 1.93 (3H, d, J = 7.0 Hz), 1.82–1.76 (2H, m), 0.89 (9H, s), 0.026 (6H, d, J = 5.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.2, 172.8, 165.6, 136.6, 134.9, 133.5, 131.3, 129.0, 128.8, 128.7, 128.6, 126.8, 126.5, 126.1, 124.1, 123.6, 122.8, 119.5, 113.9, 62.4, 58.3, 53.7, 50.7, 44.6, 32.6, 25.9, 23.0, 19.0, 18.2, –5.4; IR (KBr) 1717, 1133 cm^{-1}; MS (EI) *m/z* 624 (M^+); HRMS (EI) *m/z* calcd for $C_{37}H_{44}N_2O_5Si$ (M^+) 624.3020, found 624.3026.

Alcohol S3. To a stirred solution of the pyrrole **32** (246 mg, 0.394 mmol) in THF (1.2 mL) were added acetic acid (71.0 mg, 1.18 mmol) and TBAF (1 M in THF, 1.2 mL, 1.2 mmol) at 0 °C. After stirred for 12 h at room temperature, the reaction was quenched with sat. aqueous $NaHCO_3$ and the aqueous phase was extracted with AcOEt. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and concentrated in *vacuo*. The residue was purified by flash column chromatography on silica gel (eluent: hexane/AcOEt = 40:60 ~ CH_2Cl_2/MeOH = 10:1) to afford the alcohol **S3** (161 mg, 83%) as a colorless solid.

R_f = 0.42 (hexane/AcOEt = 30:70); mp 225–226 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.26 (8H, m), 6.97 (2H, d, J = 6.8 Hz), 6.82 (1H, d, J = 17.2 Hz), 6.75–6.66 (1H, m), 6.30 (1H, dd, J = 16.0, 4.8 Hz), 6.24 (1H, d, J = 16.0 Hz), 5.42 (1H, dd, J = 8.0, 4.8 Hz), 4.49 (1H, d, J = 8.8 Hz), 4.45 (1H, dd, J = 8.8, 8.0 Hz), 3.86 (3H, s), 3.54 (2H, t, J = 5.6 Hz), 3.09–3.04 (1H, m), 2.84–2.81 (1H, m), 2.73 (1H, br s), 1.91 (3H, d, J = 6.0 Hz), 1.87–1.86 (1H, m), 1.72–1.69 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 172.7, 166.5, 136.2, 134.7, 133.8, 131.2, 129.1, 128.8, 128.7, 126.8, 126.4, 126.3, 124.7, 123.4, 122.7, 119.0, 114.6, 60.8, 58.6, 53.6, 51.1, 44.5, 31.9, 21.8, 19.0; IR (KBr) 3540, 1713, 1680 cm^{-1}; MS (EI) *m/z* 510 (M^+); HRMS (FAB) *m/z* calcd for $C_{31}H_{31}N_2O_5$ (M^++1) 511.2233, found 511.2266.

Iodide 33. To a stirred solution of PPh_3 (77.2 mg, 0.294 mmol) in CH_2Cl_2 (0.49 mL) were added iodine (74.6 mg, 0.294 mmol), imidazole (20.9 mg, 0.294 mmol) at room temperature. After stirred for 0.5 h at the same temperature, the solution was diluted and added the alcohol **S3** (50.2 mg, 0.979 mmol) at room temperature. After stirred for 0.5 h at the same temperature, the reaction was quenched with sat. aqueous $NaHCO_3$ and the aqueous phase was extracted with CH_2Cl_2. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and concentrated in *vacuo*. The residue was purified by flash column chromatography on silica gel (eluent: hexane/AcOEt = 70:30 ~ CH_2Cl_2 only) to afford the iodide **33** (49.9 mg, 81%) as a colorless solid.

R_f = 0.56 (hexane/AcOEt = 70:30); mp 199–201 °C (decomp.); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–7.26 (7H, m), 6.98 (2H, d, *J* = 8.0 Hz), 6.88 (1H, d, *J* = 16.0 Hz), 6.71 (1H, dq, *J* = 16.0, 6.4 Hz), 6.30–6.29 (2H, m), 5.44 (1H, dd, *J* = 9.2, 4.8 Hz), 4.50 (1H, d, *J* = 8.8 Hz), 4.45 (1H, dd, *J* = 9.2, 8.8 Hz), 3.84 (3H, s), 3.15 (2H, t, *J* = 6.8 Hz), 3.01–2.94 (1H, m), 2.85–2.78 (1H, m), 2.08–2.01 (2H, m), 1.90 (3H, d, *J* = 4.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ□173.0, 172.6, 165.5, 134.8, 134.7, 134.0, 131.2, 128.9, 128.8, 128.7, 126.9, 126.5, 126.4, 124.5, 123.4, 122.6, 119.5, 114.5, 58.8, 53.5, 50.9, 44.6, 32.9, 27.3, 19.0, 6.5; IR (KBr) 1715, 1697, 1498, 1443, 1377, 1134 cm^{-1}; MS (EI) *m/z* 620 (M^+); HRMS (FAB) *m/z* calcd for $C_{31}H_{30}IN_2O_4$ (M^++1) 621.1251, found 621.1221.

Amine 34. To a stirred solution of the iodide **33** (30.0 mg, 0.0483 mmol) in THF (0.39 mL) was added Me_2NH (2 M in THF, 97.0 μL, 0.193 mmol) at room temperature. After stirred for 12 h, the reaction was quenched with water and the aqueous phase was extracted with $CHCl_3$. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and concentrated in *vacuo*. The residue was purified on preparative TLC (eluent: $CHCl_3$/MeOH = 10:1) to afford the amine **34** (24.5 mg, 81%) as a colorless solid.

R_f = 0.40 ($CHCl_3$/MeOH = 10:1); mp 170–172 °C (decomp.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30–7.26 (6H, m), 7.25–7.24 (2H, m), 6.97 (2H, d, *J* = 6.4 Hz), 6.89 (1H, d, *J* = 12.8 Hz), 6.73–6.68 (1H, m), 6.31 (1H, dd, *J* = 12.8, 6.4 Hz), 6.26 (1H, d, *J* = 12.8 Hz), 5.49–5.46 (1H, m), 4.49 (1H, d, *J* = 6.8 Hz), 4.43 (1H, dd, *J* = 7.2, 6.8 Hz), 3.83 (3H, s), 2.92–2.86 (1H, m), 2.72–2.66 (1H, m), 2.24 (2H, t, *J* = 5.6 Hz), 2.14 (6H, s), 1.90 (3H, d, *J* = 4.8 Hz), 1.77–1.72 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.1, 172.8, 165.6, 136.6, 134.8, 133.7, 131.3, 129.1, 128.9, 128.7, 126.9, 126.5, 126.3, 124.2, 123.6, 122.7, 119.4, 114.0, 58.9, 58.6, 53.6, 50.8, 45.1, 44.6, 27.3, 24.1, 19.1; IR (KBr) 1712, 1696 cm^{-1}; MS (EI) *m/z* 537 (M^+); HRMS (FAB) *m/z* calcd for $C_{33}H_{36}N_3O_4$ (M^++1) 538.2706, found 538.2715.

Olefin 35. To a stirred solution of the amine **34** (21.9 mg, 0.0407 mmol) in CH_2Cl_2 (0.70 mL) were added *m*–CPBA (≤77% purity, 10.0 mg, 0.0448 mmol) and K_2CO_3 (8.4 mg, 0.0611 mmol) at –78 °C. After stirred at the same temperature for 3 h and at room temperature for 0.5 h, the reaction mixture was filtered through a pad of $MgSO_4$, the filtrate was concentrated in *vacuo*. The residue was purified through a short

pad of silica gel (eluent: $CHCl_3$/MeOH = 10:1 ~ CH_2Cl_2/MeOH 1:1) to give a crude mixture of *N*–oxide [22.0 mg, R_f = 0.21 ($CHCl_3$/MeOH = 10:1)]. A solution of the above crude *N*–oxide in xylene (0.40 mL) was heated at 100 °C for 21 h and the reaction mixture was concentrated in *vacuo*. The residue was purified by flash column chromatography on silica gel (eluent: hexane/AcOEt = 70:30 ~ $CHCl_3$/MeOH = 10:1) to afford the olefin **35** (8.5 mg, 43% for 2 steps) as a colorless solid.

R_f = 0.41 (hexane/AcOEt = 70:30); mp 217–221 °C (decomp.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29–7.26 (3H, m), 7.25–7.22 (4H, m), 6.95–6.93 (2H, m), 6.87 (1H, d, *J* = 13.2 Hz), 6.72–6.66 (1H, m), 6.27 (1H, dd, *J* = 13.2, 4.0 Hz), 6.21 (1H, d, *J* = 13.2 Hz), 5.86–5.78 (1H, m), 5.36 (1H, dd, *J* = 7.6, 4.0 Hz), 4.97 (2H, dd, *J* = 14.0, 6.8 Hz), 4.47 (1H, d, *J* = 6.8 Hz), 4.42 (1H, dd, *J* = 7.6, 6.8 Hz), 3.90 (1H, dd, *J* = 12.0, 4.4 Hz), 3.82 (3H, s), 3.32 (1H, dd, *J* = 12.0, 4.4 Hz), 1.89 (3H, d, *J* = 5.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ□173.1, 172.8, 165.6, 134.9, 134.7, 133.8, 133.2, 13.1, 129.1, 128.9, 128.7, 126.9, 126.5, 126.3, 124.9, 123.3, 122.6, 119.4, 116.5, 116.1, 114.6, 58.4, 53.7, 50.8, 44.6, 30.4, 19.1; IR (KBr) 1717, 1498, 1377 cm^{-1}; MS (EI) *m/z* 492 (M^+); HRMS (FAB) *m/z* calcd for $C_{31}H_{29}N_2O_4$ (M^++1) 493.2127, found 493.2125.

Pyrroloindolizidine 36. A solution of the olefin **35** (10.8 mg, 0.0219 mmol) and Hoveyda–Grubbs catalyst 2nd generation (2.7 mg, 0.00439 mmol) was heated in refluxing CH_2Cl_2 (0.55 mL) afforded the pyrroloindolizidine **36** (7.3 mg, 86%) as a yellow solid.

R_f = 0.20 (hexane/AcOEt = 70:30); mp 105–109 °C (decomp.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41–7.38 (2H, m), 7.34–7.31 (1H, m), 7.13 (2H, d, *J* = 6.0 Hz), 6.84 (1H, d, *J* = 12.8 Hz), 6.58 (1H, d, *J* = 8.0 Hz), 6.29 (1H, dq, *J* = 12.8, 5.6 Hz), 6.12–6.10 (1H, m), 4.90–4.87 (1H, m), 4.75 (1H, d, *J* = 5.2 Hz), 4.19 (1H, dd, *J* = 5.6, 5.6 Hz), 3.84–3.80 (1H, m), 3.80 (3H, s), 3.40–3.34 (1H, m), 1.90 (3H, d, *J* = 5.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.8, 170.4, 165.6, 131.3, 129.8, 129.0, 128.6, 126.5, 126.3, 122.0, 121.6, 121.1, 120.9, 111.9, 53.2, 52.3, 50.7, 45.8, 25.8, 18.9; IR (KBr) 1719, 1378, 1144 cm^{-1}; MS (EI) *m/z* 388 (M^+); HRMS (EI) *m/z* calcd for $C_{23}H_{20}N_2O_4$ (M^+) 388.1423, found 388.1453.

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9. The relative stereochemistries in **17** were assigned by ^{1}H NMR analysis on methine protons, whose chemical shifts and coupling patterns shown good accordance with the similar compound in our previous report.[7]
10. Although the lower stability of imine **13** cannot be excluded for the reason of the poor result, our previous studies suggested the presence of desiccant ($MgSO_4$, MS 4A) avoided our gold catalyzed reactions.
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