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Gold-Catalyzed Cycloisomerization of α-Aminoallenes to 3-Pyrrolines – Optimization and Mechanistic Studies

Nobuyoshi Morita[a][‡] and Norbert Krause*[a]

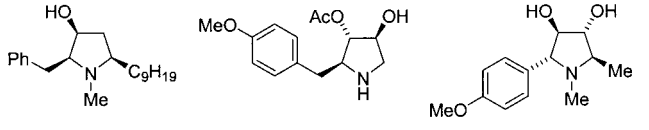
Dedicated to the memory of Professor Oyo Mitsunobu (1934–2003)

Keywords: α-Aminoallenes / Chirality transfer / Cycloisomerization / Gold / Heterocycles / Homogeneous catalysis / Intramolecular hydroamination / 3-Pyrrolines

The gold-catalyzed cycloisomerization of various α-aminoallenes affords the corresponding 3-pyrrolines in good to high chemical yields and – if the amino group is unprotected – with complete axis-to-center chirality transfer. Diminished levels of chirality transfer were observed in cases of *N*-protected substrates, which may be the result of partial epimerization of the allene in the presence of the gold precatalyst. The low reactivity of the intramolecular hydroamination of unprotected α-aminoallenes with $AuCl_3$ was improved by use of gold(I) halides as the precatalyst. Mechanistic studies suggest that a gold(I) compound (formed by oxidation of the aminoallene) is the catalytically active species even if the reaction is started with a gold(III) precatalyst.

Introduction

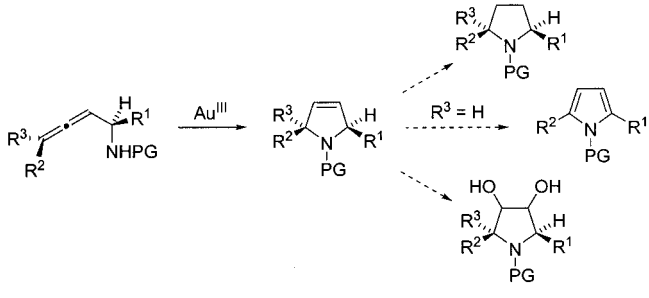
The efficient synthesis of functionalized pyrrolines and pyrrolidines is of great importance in the field of natural products and pharmaceutically active compounds because of their powerful and diverse biological activities (Figure 1).[1] Examples of pyrrolidine alkaloids include preussin, anisomycin (antifungal activity[2]), codonopsinine (hypotensive activity[3]), lentiginosine, swainsonine, and alexine (enzyme inhibitors[4]). Moreover, the 3-pyrroline skeleton has been found included in MAO inhibitors,[5] NMDA receptor agonists,[6] a k-agonist,[7] and tumor inhibitors.[8]



Preussin (Anti-fungal activity) **Anisomycin** (Anti-fungal activity) **Codonopsinine** (Hypotensive activity)

Figure 1. Naturally occurring pyrrolidines.

It is therefore not surprising that numerous pathways for the synthesis of substituted pyrrolines and pyrrolidines have been developed,[1] much work in recent years having focused on metal-mediated or catalyzed approaches. For control over the relative and absolute configurations of the stereogenic centers in positions 2 and/or 5 of the heterocycles, the cyclization/cycloisomerization of sterically defined α-aminoallenes is particularly promising, and transition metals such as Pd^0/Pd^{II},[9] Ag^I,[10] Hg^{II},[11] and Ru^{III},[10a] as well as organolanthanides,[12] have been used for this purpose. In connection with our ongoing activities devoted to the gold-catalyzed[13] cycloisomerization of functionalized allenes (such as α-hydroxyallenes[14] and α-thioallenes[15]) we have recently demonstrated that gold(III) salts are efficient precatalysts for the intramolecular hydroamination of α-aminoallenes to afford 3-pyrrolines (Scheme 1).[16–18] Since 3-pyrrolines can easily be transformed into pyrrolidines or pyrroles[19] with various functional groups through re-



Scheme 1. Gold-catalyzed cycloisomerization of α-aminoallenes and subsequent transformations of the 3-pyrrolines formed.

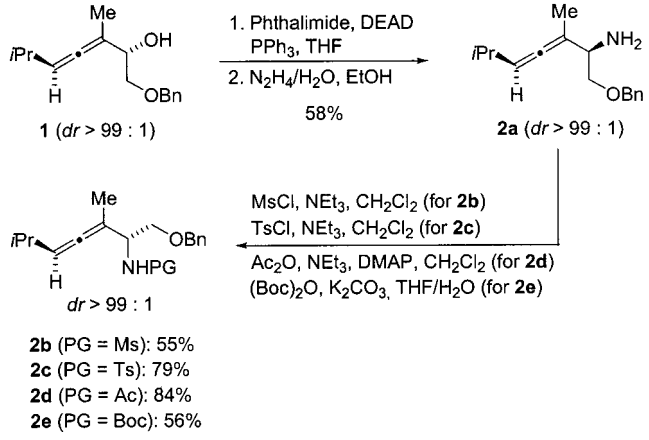
[a] Dortmund University, Organic Chemistry II,
Otto-Hahn-Strasse 6, 44227 Dortmund, Germany
Fax: +49-231-755-3884
E-mail: norbert.krause@uni-dortmund.de
[‡] New address: Showa Pharmaceutical University,
3-3165 Higashi-tamagawagakuen, Machida, Tokyo 194-8543, Japan

duction, oxidation, and other known reactions, this method opens up a new route to the stereoselective synthesis of pyrrolidine and indolizidine alkaloids.

In this paper we present recent results of investigations dedicated towards the optimization of the gold-catalyzed cycloisomerization of α-aminoallenes to 3-pyrrolines, as well as experimental evidence for the catalytically active gold species and the reaction mechanism.

Results and Discussion

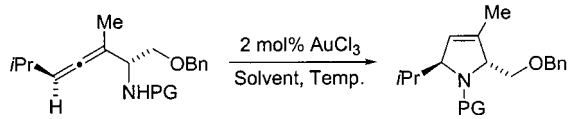
The synthesis of the starting materials for our study, the α-aminoallenes **2**, is shown in Scheme 2. The diastereomerically pure hydroxyallene **1** (obtained through the *anti*-selective S_N2'-substitution reaction between a propargylic oxirane and a magnesium cyanocuprate[14]) was converted in good yield and with complete inversion into the α-aminoallene **2a** through a Mitsunobu reaction with phthalimide, followed by hydrazinolysis.[20] The amino group of **2a** was protected with various protecting groups under standard conditions. The α-aminoallenes **2f**–**h** (vide infra) were also obtained from the corresponding hydroxyallenes[14] through Mitsunobu reactions.



Scheme 2. Synthesis of α-aminoallenes **2**.

We started our study by treating the diastereomerically pure α-aminoallenes **2a**–**e** with $AuCl_3$ (2 mol-%) in dry CH_2Cl_2 at room temperature, conditions highly efficient for the cyclization of α-hydroxyallenes.[14] Indeed, the desired 3-pyrrolines **3a**–**e** were obtained in good to excellent yields (69–95%; see Table 1). The reactions were complete at room temperature after 30 min in the cases of the *N*-protected aminoallenes **2b**–**2e** (Entries 2, 3, 6, 7), whereas the unprotected substrate required much longer reaction times (Entry 1). A slight deterioration in the stereoselectivity was observed during the cyclization of the sulfonylated substrates **2b** and **2c** and was not affected by the solvent or temperature (Entries 2–5). This effect was even more pronounced in the cases of the acylated aminoallenes **2d** and **2e** (Entries 6 and 7). Only the unprotected aminoallene **2a** reacted with complete chirality transfer to afford the diastereomerically pure 3-pyrroline **3a** (Entry 1).

Table 1. $AuCl_3$-catalyzed cycloisomerization of α-aminoallenes **2** to 3-pyrrolines **3**.



2 **3**

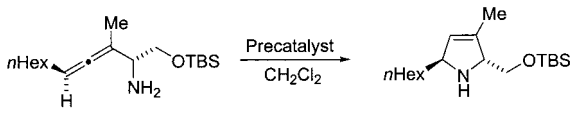
Entry	2	PG	Solvent	Temp.	Time	3 Yield	dr
1	**2a**	H	CH_2Cl_2	r.t	5 days	**3a** 74%	> 99 : 1
2	**2b**	Ms	CH_2Cl_2	r.t	30 min	**3b** 77%	94 : 6
3	**2c**	Ts	CH_2Cl_2	r.t	30 min	**3c** 93%	95 : 5
4	**2c**	Ts	CH_2Cl_2	0°C	1 h	**3c** 95%	96 : 4
5	**2c**	Ts	THF	r.t	1.5 h	**3c** 95%	93 : 7
6	**2d**	Ac	CH_2Cl_2	r.t	30 min	**3d** 80%	70 : 30
7	**2e**	Boc	CH_2Cl_2	r.t	30 min	**3e** 69%	46 : 54

The long reaction time required for complete conversion of the unprotected α-aminoallene **2a** prompted us to optimize the reaction conditions for the cyclization of model substrate **2f** by variation of the gold precatalyst and the reaction temperature, and also by employment of additives (Table 2). With 2 mol-% of $AuCl_3$ or $AuBr_3$ in dichloromethane, 5 d at room temperature or 8 h at reflux were necessary to induce complete and clean conversion of the aminoallene into the product **3f** (71–83% yield, Entries 1, 2, 8). Increasing the catalyst loading to 5 mol-% produced a decreased reaction time of 2 d (Entries 3, 9), whilst the use of 2,2′-bipyridine or 3-hydroxypropionitrile as additives seemed to accelerate the reaction slightly, but the yield of 3-pyrroline **3f** was somewhat lower (Entries 4–7). Whereas the (phosphane)gold(I) precatalyst Ph_3PAuCl and the cationic complex **A**[21] did not afford any product (Entries 13, 15), the cationic catalyst formed from Ph_3PAuCl and $AgSbF_6$ gave a reaction time similar to those achieved with $AuCl_3$ and $AuBr_3$ (Entry 14). The breakthrough was achieved with the use of the simple gold(I) halides AuCl and AuI, which brought about a dramatic acceleration of the intramolecular hydroamination, relative to the use of Au^{III} precatalysts, to give **3f** in 61–76% yield after just 1–6 h reaction times (Entries 10–12). All transformations took place with complete axis-to-center chirality transfer.

To examine the scope of the gold-catalyzed intramolecular hydroamination of α-aminoallenes further and to compare the reactivities of Au^{I} and Au^{III} precatalysts, we extended our investigation to substrates **2a**, **2g**, and **2h**. These were efficiently converted into the corresponding 3-pyrrolines **3** by both types of gold precatalyst in good to high chemical yields with complete axis-to-center chirality transfer (Table 3). In all cases examined the reaction times could be reduced from several days to a few hours at room temperature by using AuCl or AuI instead of $AuCl_3$.

A possible explanation for this experimental result may be that it is a gold(I) compound that acts as the catalytically active species even if a gold(III) precatalyst is employed; in

Table 2. Optimization of the gold-catalyzed cycloisomerization of α-aminoallene **2f** to 3-pyrroline **3f**.



2f (*dr* = 85 :15) **3f** (*dr* = 85 : 15)

Entry	Precatalyst (mol%)	Additive (mol%)	Temp.	Time	Yield
1	$AuCl_3$ (2)	-	r.t	5 days	82%
2	$AuCl_3$ (2)	-	reflux	8 h	83%
3	$AuCl_3$ (5)	-	r.t	2 days	80%
4	$AuCl_3$ (2)	2,2'-bipyridine (4)	r.t	3 days	62%
5	$AuCl_3$ (2)	2,2'-bipyridine (4)	reflux	6 h	67%
6	$AuCl_3$ (2)	$HO(CH_2)_2CN$ (4)	r.t	3 days	64%
7	$AuCl_3$ (2)	$HO(CH_2)_2CN$ (4)	reflux	6 h	67%
8	$AuBr_3$ (2)	-	r.t	5 days	71%
9	$AuBr_3$ (5)	-	r.t	2 days	73%
10	AuCl (2)	-	r.t	6 h	61%
11	AuCl (5)	-	r.t	1 h	70%
12	AuI (2)	-	r.t	4 h	76%
13	Ph_3PAuCl (5)	-	r.t	7 days	no reaction
14	Ph_3PAuCl (4)	$AgSbF_6$ (6)	r.t	3 days	64%
15	**A** (2)	-	r.t	7 days	no reaction

Precatalyst **A**:

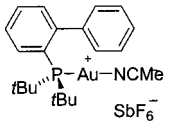
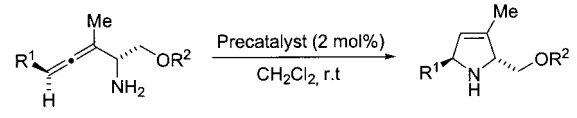


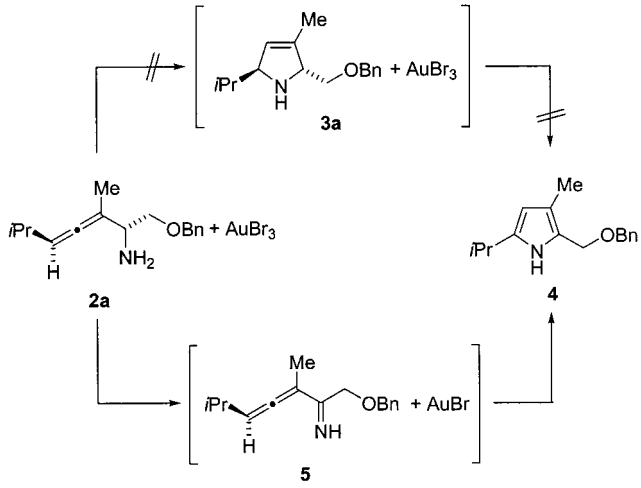
Table 3. Comparison of Au^I and Au^{III} precatalysts in the cycloisomerization of unprotected α-aminoallenes.



2 **3**

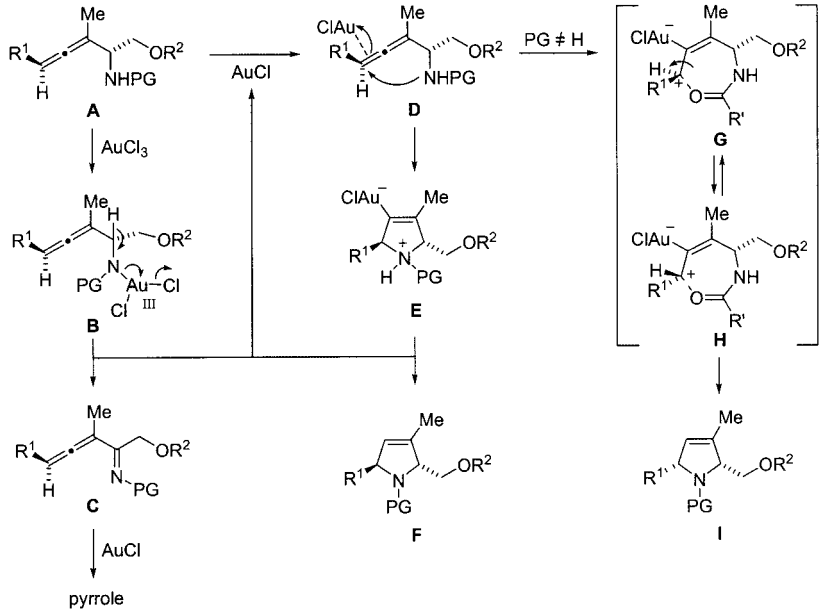
Entry	2	R^1	R^2	*dr*	Precatalyst	Time	3	Yield	*dr*
1	**2a**	*i*Pr	Bn	99 : 1	$AuCl_3$	5 days	**3a**	74%	99 : 1
2	**2a**	*i*Pr	Bn	99 : 1	AuCl	6 h	**3a**	71%	99 : 1
3	**2f**	*n*Hex	TBS	85 : 15	$AuCl_3$	5 days	**3f**	82%	85 : 15
4	**2f**	*n*Hex	TBS	85 : 15	AuCl	6 h	**3f**	61%	85 : 15
5	**2f**	*n*Hex	TBS	85 : 15	AuI	4 h	**3f**	76%	85 : 15
6	**2g**	Me	Bn	90 : 10	$AuCl_3$	5 days	**3g**	71%	90 : 10
7	**2g**	Me	Bn	90 : 10	AuCl	6 h	**3g**	60%	90 : 10
8	**2h**	Ph	TBS	>99 : 1	$AuCl_3$	5 days	**3h**	79%	>99 : 1
9	**2h**	Ph	TBS	>99 : 1	AuCl	6 h	**3h**	69%	>99 : 1

such a case a rather slow reduction of Au^{III} to Au^I would be followed by a rather fast cyclization. In order to gather experimental evidence in support of this assumption, we treated α-aminoallene **2a** with 1 equiv. of $AuBr_3$[22] in THF and looked for a possible oxidation product of the substrate, which would indicate reduction of the gold precatalyst (Scheme 3). We obtained a product mixture containing the pyrrole **4** together with other unidentified, probably polymeric, products.[23] Analogous treatment of the 3-pyrroline **3a** with 1 equiv. of $AuBr_3$ induced complete decomposition of the substrate without formation of pyrrole **4**. Our interpretation of these results is that the intramolecular hydroamination of α-aminoallenes to afford 3-pyrrolines is catalyzed by gold(I), but not by gold(III); if a gold(III) precatalyst is used, this is reduced by the substrate to form an allenic imine **5** (and possibly other oxidation products), which (analogously to allenic ketones[24]) is cyclized to the pyrrole **4**.[25] This explanation is in line with our finding that the cyclization of α-thioallenes with gold(III) precatalysts also affords oxidation products of the substrates (disulfides) as side products, indicating that a gold(I) compound is the catalytically active species.[15]



Scheme 3. Treatment of **2a** and **3a** with stoichiometric amounts of $AuBr_3$.

A comprehensive mechanistic proposal for the gold-catalyzed cycloisomerization of α-aminoallenes to 3-pyrrolines is shown in Scheme 4. We assume that the catalytically active gold(I) species activates the "terminal" allenic double bond of the substrate **A** to give intermediate **D**, which undergoes an intramolecular nucleophilic attack by the nitrogen atom via an S_N2-type transition state to afford the zwitterionic intermediate **E**, and that this is transformed into the 3-pyrroline **F** by protodemetalation with complete axis-to-center chirality transfer. In the case of the *N*-protected aminoallenes **2b–e**, however, oxygen in the protecting group could stabilize the zwitterionic complex **G** by coordination, and the cyclization would proceed with partial isomerization (through single-bond rotation) to complex **H** to afford a mixture of the diastereomeric heterocycles **F** and **I**. At present it is not clear why this pathway is more pronounced for the acetyl/Boc-protected substrates **2d/e** than for the sulfonamides **2b/c**. If a gold(III) precatalyst is used, coordination to the nitrogen atom of **A** should provide the complex **B**, which could undergo elimination of HCl to give the gold(I) catalyst and the imine **C**, the latter then being cyclized to the corresponding pyrrole.



Scheme 4. Plausible mechanism of the gold-catalyzed cycloisomerization of α-aminoallenes to 3-pyrrolines.

Conclusions

We have developed an efficient gold-catalyzed cycloisomerization reaction of α-aminoallenes to give the corresponding 3-pyrrolines, taking place with complete axis-to-center chirality transfer if the amino group is unprotected. In cases involving *N*-protected substrates, an interesting dependence of the chirality transfer on the protecting group was observed. Gold(I) precatalysts such as AuCl and AuI are extremely reactive and dramatically shorten the reaction times for the intramolecular hydroamination of unprotected α-aminoallenes. Mechanistic studies with stoichiometric amounts of $AuBr_3$ suggest that a gold(I) compound (formed by oxidation of the aminoallene) is the catalytically active species even if the reaction is started with a gold(III) precatalyst. Application of the method in alkaloid synthesis is now being studied in our laboratories.

Experimental Section

General Information: ^1H and ^{13}C NMR spectra were recorded with Bruker DRX 400 or DRX 500 spectrometers at room temperature in $CDCl_3$ or C_6D_6 as solvents. Chemical shifts were determined relative to the residual solvent peaks ($CHCl_3$: δ = 7.26 ppm for protons, δ = 77.16 ppm for carbon atoms; C_6H_6: δ = 7.16 ppm for protons, δ = 128.06 ppm for carbon atoms). The signals of the major component of a product mixture are marked with asterisks (*). GC analyses were carried out with a Carlo Erba GC 8000 gas chromatograph with helium as the carrier gas and on an OV-1701 capillary column. IR spectra were obtained with a Perkin–Elmer 1600 FT-IR spectrometer. Mass spectra were obtained with a JEOL SX102A (FAB) spectrometer. All products were >98% pure as determined by GC analysis and NMR spectroscopy.

Preparation of Unprotected α-Aminoallenes: Triphenylphosphane (PPh_3) and phthalimide were added at room temperature under argon to a solution of the α-hydroxyallene[14] in THF. Diethyl azodicarboxylate (DEAD) was added dropwise to the reaction mixture at 0 °C. After complete consumption (the reaction was monitored by thin layer chromatography), the solvent was removed in vacuo and the crude product was purified by column chromatography on silica gel to afford the corresponding phthalimide. Hydrazine hydrate was added slowly at room temperature to a solution of the phthalimide in EtOH. The reaction mixture was heated to reflux for 2–3 h, resulting in the formation of a white precipitate. Concentrated HCl solution (1–2 mL) was added to the mixture at 0 °C and the precipitate was removed by filtration. The filtrate was cooled to 0 °C and NaOH solution (1 N) was added slowly to make the filtrate basic (pH > 10). The filtrate was extracted with EtOAc and the combined organic phases were washed with brine and dried with sodium sulfate. The solvent was removed in vacuo and the crude product was purified by column chromatography (CH_2Cl_2/MeOH, 10:1) on silica gel to afford the corresponding α-aminoallene.

1-(Benzyloxymethyl)-2,5-dimethylhexa-2,3-dienylamine (2a): Treatment of α-hydroxyallene **1** (1.8 g, 7.3 mmol) with PPh_3 (3.8 g, 15 mmol), DEAD (2.7 mL, 15 mmol), and phthalimide (2.1 g, 15 mmol) in THF (50 mL) afforded the corresponding phthalimide (1.9 g, 68%) as a colorless oil. Treatment of the phthalimide (0.76 g, 2.0 mmol) with hydrazine hydrate (198 μL, 4.0 mmol) in EtOH (20 mL) gave the α-aminoallene **2a** (0.43 g, 86%) as a light brown liquid. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.22 (m, 5 H), 5.20–5.15 (m, 1 H), 4.53 (s, 2 H), 3.58 (dd, *J* = 9.0, 3.5 Hz, 1 H), 3.45–3.39 (m, 1 H), 3.32–3.28 (m, 1 H), 2.30–2.20 (m, 1 H), 1.71 (d, *J* = 2.8 Hz, 3 H), 0.97 (d, *J* = 6.8 Hz, 3 H), 0.97 (d, *J* = 6.8 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.2, 138.4, 128.5, 127.8, 127.7, 100.8, 74.3, 73.3, 72.5, 53.8, 28.3, 22.8, 22.7, 17.0 ppm. IR (neat): $\tilde{\nu}$ = 3371, 3302, 3030, 2958, 2868, 1963 cm^{-1}. HRMS (FAB): calcd. for $C_{16}H_{23}NO$ $[M + H]^+$: *m*/*z* = 246.1858; found: *m*/*z* = 246.1859.

1-(*tert*-Butyldimethylsilyloxymethyl)-2-methyldeca-2,3-dienylamine (2f): Treatment of 1-(*tert*-butyldimethylsilyloxy)-3-methylundeca-3,4-dien-2-ol (1.6 g, 5.1 mmol, *dr* = 85:15) with PPh_3 (2.7 g, 10 mmol), DEAD (1.9 mL, 10 mmol), and phthalimide (1.5 g, 10 mmol) in THF (90 mL) afforded the corresponding phthalimide (1.7 g, 75%, *dr* = 85:15 by GC and NMR analysis) as a colorless oil. Treatment of the phthalimide (1.5 g, 3.4 mmol) with hydrazine

hydrate (330 μL, 6.8 mmol) in EtOH (40 mL) gave the α-aminoallene **2f** (0.88 g, 83%, *dr* = 85:15 by GC and NMR analysis) as a light brown liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.21/5.17* (brs, 1 H), 3.75–3.70*/3.70–3.65 (m, 1 H), 3.42–3.38 (m, 1 H), 3.30–3.20 (m, 1 H), 2.00–1.94 (m, 2 H), 1.70 (d, *J* = 2.8 Hz, 3 H), 1.40–1.22 (m, 8 H), 0.88 (s, 9 H), 0.87 (t, *J* = 7.0 Hz, 3 H), 0.04 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.9*, 199.9, 93.5*, 93.3*, 67.0*, 55.5*, 31.8*, 29.4*, 29.4, 29.3*, 29.3, 28.9*, 26.0, 26.0*, 22.8*, 18.4, 18.4*, 17.2, 17.0*, 14.2*, –5.2*, –5.3* ppm. IR (neat): $\tilde{\nu}$ = 3374, 2955, 2927, 1963 cm^{-1}. HRMS (FAB): calcd. for $C_{18}H_{37}NOSi$ [M + H]$^+$: *m*/*z* = 312.2723; found: *m*/*z* = 312.2709.

1-(Benzyloxymethyl)-2-methylpenta-2,3-dienylamine (2g): Treatment of 1-benzyloxy-3-methylhexa-3,4-dien-2-ol (0.83 g, 3.8 mmol, *dr* = 90:10) with PPh_3 (2.0 g, 7.6 mmol), DEAD (1.4 mL 7.6 mmol), and phthalimide (1.1 g, 7.6 mmol) in THF (30 mL) afforded the corresponding phthalimide (0.59 g, 45%, *dr* = 90:10 by GC and NMR analysis) as a colorless oil. Treatment of the phthalimide (0.30 g, 0.86 mmol) with hydrazine hydrate (85 μL, 1.7 mmol) in EtOH (7 mL) gave the α-aminoallene **2g** (0.15 g, 80%, *dr* = 90:10 by GC and NMR analysis) as a light brown liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30–7.07 (m, 5 H), 5.22–5.18/5.10–5.00* (m 1 H), 4.32 (s, 2 H), 3.49 (dd, *J* = 8.5, 4.0 Hz, 1 H), 3.47–3.40 (m, 1 H), 3.31–3.26 (m, 1 H), 1.71/1.70* (d, *J* = 2.7 Hz, 3 H), 1.53 (d, *J* = 6.8 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 202.2*, 202.1, 139.2*, 128.6*, 127.8*, 127.7*, 127.6*, 87.1*, 75.0*, 73.2*, 54.4*, 16.6*, 16.5* ppm. IR (neat): $\tilde{\nu}$ = 3360, 3305, 3025, 2957, 1963 cm^{-1}. HRMS (FAB): calcd. for $C_{14}H_{19}NO$ [M + H]$^+$: *m*/*z* = 218.1545; found: *m*/*z* = 218.1516.

1-(*tert*-Butyldimethylsilyloxymethyl)-2-methyl-4-phenylbuta-2,3-dienylamine (2h): Treatment of 1-(*tert*-butyldimethylsilyloxy)-3-methyl-5-phenylpenta-3,4-dien-2-ol (0.80 g, 2.6 mmol) with PPh_3 (1.4 g, 5.3 mmol), DEAD (0.96 mL, 5.3 mmol), and phthalimide (0.77 g, 5.3 mmol) in THF (40 mL) afforded the corresponding phthalimide (0.48 g, 42%) as a colorless oil. Treatment of the phthalimide (0.48 g, 1.1 mmol) with hydrazine hydrate (108 μL, 2.2 mmol) in EtOH (15 mL) gave the α-aminoallene **2h** (0.26 g, 77%) as a light brown liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30–7.15 (m, 5 H), 6.17–6.15 (m, 1 H), 3.77 (dd, *J* = 9.8, 4.0 Hz, 1 H), 3.52 (dd, *J* = 9.8, 6.8 Hz, 1 H), 3.45–3.38 (m, 1 H), 1.85 (d, *J* = 2.8 Hz, 3 H), 0.91 (s, 9 H), 0.07 (s, 3 H), 0.06 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 202.5, 135.3, 128.7, 126.9, 126.7, 96.3, 67.0, 56.2, 26.1, 26.0, 18.4, 16.5, –5.1, –5.2 ppm. IR (neat): $\tilde{\nu}$ = 3374, 3305, 3053, 2956, 1964 cm^{-1}. HRMS (FAB): calcd. for $C_{18}H_{29}NOSi$ [M + H]$^+$: *m*/*z* = 304.2097; found: *m*/*z* = 304.2073.

Preparation of Protected α-Aminoallenes

***N*-[1-(Benzyloxymethyl)-2,5-dimethylhexa-2,3-dienyl]methanesulfonamide (2b):** Triethylamine (63 μL, 0.49 mmol) and MsCl (38 μL, 0.49 mmol) were added at 0 °C to a solution of the α-aminoallene **2a** (100 mg, 0.41 mmol) in CH_2Cl_2 (5 mL). The reaction mixture was stirred at room temperature for 3 h and was then poured into water and extracted with CH_2Cl_2. The combined organic phases were washed with brine and dried with sodium sulfate, the solvent was removed by rotary evaporation, and the crude product was purified by column chromatography (cyclohexane/ethyl acetate, 4:1) on silica gel to afford the product **2b** (72 mg, 55%) as a colorless oil. ^{1}H NMR (400 MHz, C_6D_6): δ = 7.18–7.07 (m, 5 H), 5.13–5.10 (m, 1 H), 4.93 (brd, *J* = 8.5 Hz, 1 H), 4.21 (ABq, *J* = 12.0 Hz, 2 H), 4.14–4.08 (m, 1 H), 3.39 (dd, *J* = 9.5, 4.5 Hz, 1 H), 3.28 (dd, *J* = 9.5, 7.0 Hz, 1 H), 3.14 (s, 3 H), 2.21–2.13 (m, 1 H), 1.67 (d, *J* = 3.0 Hz, 3 H), 0.95 (d, *J* = 6.8 Hz, 6 H) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ = 200.0, 138.4, 128.7, 128.0, 127.9, 101.2, 100.2, 73.2, 72.2, 56.2, 41.7, 28.6, 22.7, 22.6, 16.7 ppm. IR (KBr): $\tilde{\nu}$ = 3374, 3054, 2962, 1965 cm^{-1}. HRMS (FAB): calcd. for $C_{17}H_{25}NO_3S$ [M + H]$^+$: *m*/*z* = 324.1633; found: *m*/*z* = 324.1626.

***N*-[1-(Benzyloxymethyl)-2,5-dimethylhexa-2,3-dienyl]-4-methylbenzenesulfonamide (2c):** Triethylamine (63 μL, 0.49 mmol) and TsCl (93 mg, 0.49 mmol) were added at 0 °C to a solution of the α-aminoallene **2a** (100 mg, 0.41 mmol) in CH_2Cl_2 (5 mL). The reaction mixture was stirred at room temperature overnight and was then poured into water and extracted with CH_2Cl_2. The combined organic phases were washed with brine and dried with sodium sulfate, the solvent was removed by rotary evaporation, and the crude product was purified by column chromatography (cyclohexane/ethyl acetate, 10:1) on silica gel to afford the product **2c** (128 mg, 79%) as a light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74 (d, *J* = 8.0 Hz, 2 H), 7.38–7.20 (m, 7 H), 5.22–5.19 (m, 1 H), 4.91 (brd, *J* = 7.3 Hz, 1 H), 4.40 (s, 2 H), 3.88–3.83 (m, 1 H), 3.50 (dd, *J* = 9.8, 5.0 Hz, 1 H), 3.40 (dd, *J* = 9.8, 5.0 Hz, 1 H), 2.42 (s, 3 H), 2.26–2.18 (m, 1 H), 1.61 (d, *J* = 3.0 Hz, 3 H), 0.95 (d, *J* = 6.8 Hz, 3 H), 0.94 (d, *J* = 6.8 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.9, 143.3, 137.8, 137.7, 129.6, 128.5, 127.8, 127.7, 127.3, 101.3, 99.5, 73.2, 71.2, 55.8, 28.2, 22.6, 22.6, 21.7, 16.5 ppm. IR (KBr): $\tilde{\nu}$ = 3363, 3054, 2961, 1967 cm^{-1}. HRMS (FAB): calcd. for $C_{23}H_{29}NO_3S$ [M + H]$^+$: *m*/*z* = 400.1946; found: *m*/*z* = 400.1920.

***N*-[1-(Benzyloxymethyl)-2,5-dimethylhexa-2,3-dienyl]acetamide (2d):** Triethylamine (63 μL, 0.49 mmol), acetic anhydride (46 μL, 0.49 mmol), and DMAP (2.0 mg, 0.016 mmol) were added at 0 °C to a solution of the α-aminoallene **2a** (100 mg, 0.41 mmol) in CH_2Cl_2 (5 mL). The reaction mixture was stirred at room temperature for 1 h and was then cooled to 0 °C, saturated NH_4Cl solution was slowly added, and the product was extracted with CH_2Cl_2. The combined organic phases were washed with brine and dried with sodium sulfate, the solvent was removed by rotary evaporation, and the crude product was purified by column chromatography (cyclohexane/ethyl acetate, 1:1) on silica gel to afford the product **2d** (98 mg, 84%) as a yellow solid. ^{1}H NMR (400 MHz, C_6D_6): δ = 7.25–7.06 (m, 5 H), 5.63 (brd, *J* = 8.6 Hz, 1 H), 5.18 (q, *J* = 2.8 Hz, 1 H), 4.80–4.75 (m, 1 H), 4.28 (ABq, *J* = 12.0 Hz, 2 H), 3.41 (d, *J* = 4.3 Hz, 2 H), 2.23–2.15 (m, 1 H), 1.67 (d, *J* = 3.0 Hz, 3 H), 1.61 (s, 3 H), 0.96 (d, *J* = 6.8 Hz, 3 H), 0.95 (d, *J* = 6.8 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ = 199.8, 168.3, 138.8, 128.6, 127.8, 127.9, 101.4, 101.2, 73.2, 70.8, 51.0, 28.7, 22.9, 22.8, 22.6, 17.3 ppm. IR (KBr): $\tilde{\nu}$ = 3432, 3322, 3053, 2961, 1964, 1671 cm^{-1}. HRMS (FAB): calcd. for $C_{18}H_{25}NO_2$ [M]$^+$: *m*/*z* = 287.1885; found: *m*/*z* = 287.1883.

***tert*-Butyl [1-(Benzyloxymethyl)-2,5-dimethylhexa-2,3-dienyl]carbamate (2e):** K_2CO_3 (110 mg, 0.82 mmol) and Boc_2O (107 mg, 0.49 mmol) at 0 °C were added to a solution of the α-aminoallene **2a** (100 mg, 0.41 mmol) in THF (1.5 mL) and H_2O (1.5 mL). The reaction mixture was stirred at room temperature overnight, and was then poured into saturated NH_4Cl solution and extracted with EtOAc. The combined organic phases were washed with brine and dried with sodium sulfate, the solvent was removed by rotary evaporation, and the crude product was purified by column chromatography (cyclohexane/ethyl acetate, 10:1) on silica gel to afford the product **2e** (79 mg, 56%) as a colorless oil. ^{1}H NMR (400 MHz, C_6D_6): δ = 7.21–7.05 (m, 5 H), 5.15–5.17 (m, 1 H), 4.98 (brd, *J* = 8.0 Hz, 1 H), 4.46 (brs, 1 H), 4.24 (ABq, *J* = 12.0 Hz, 2 H), 3.39 (dd, *J* = 9.5, 4.3 Hz, 1 H), 3.34 (dd, *J* = 9.5, 4.5 Hz, 1 H), 2.24–2.15 (m, 1 H), 1.65 (d, *J* = 3.0 Hz, 3 H), 1.46 (s, 9 H), 0.98 (d, *J* = 6.5 Hz, 3 H), 0.97 (d, *J* = 6.5 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ = 197.7, 153.4, 136.9, 126.6, 125.9, 125.7, 99.7, 99.4, 76.8, 71.2, 69.2, 50.7, 26.7, 26.6, 20.8, 20.6, 15.4 ppm. IR (neat): $\tilde{\nu}$ = 3435, 3053, 2961, 1967, 1745 cm^{-1}. HRMS (FAB): calcd. for $C_{21}H_{31}NO_3$ [M + H]$^+$: *m*/*z* = 346.2382; found: *m*/*z* = 346.2401.

Gold-Catalyzed Cycloisomerization of α-Aminoallenes to 3-Pyrrolines

Conditions A: A solution of $AuCl_3$ in CH_3CN (0.165 M, 2 mol-%) was added at room temperature under argon to a solution of α-aminoallene in dry CH_2Cl_2. After 5 d (the reaction was monitored by thin layer chromatography), the solvent was removed in vacuo and the crude product was subjected to SiO_2 column chromatography (CH_2Cl_2/MeOH, 10:1) to give the corresponding 3-pyrroline.

Conditions B: AuCl or AuI (2 mol-%) was added at room temperature under argon to a solution of α-aminoallene in dry CH_2Cl_2. After complete consumption (usually 4–6 h), the solvent was removed in vacuo and the crude product was subjected to SiO_2 column chromatography (CH_2Cl_2/MeOH, 10:1) to give the corresponding 3-pyrroline.

2-(Benzyloxymethyl)-5-isopropyl-3-methyl-2,5-dihydro-1*H*-pyrrole (3a): Conditions A: α-Aminoallene **2a** (42 mg, 0.17 mmol) in CH_2Cl_2 (4 mL) and a solution of $AuCl_3$ in CH_3CN (20 μL, 2 mol-%) furnished 3-pyrroline **3a** (31 mg, 74%) as a colorless oil. Conditions B: α-Aminoallene **2a** (55 mg, 0.22 mmol) in CH_2Cl_2 (6 mL) and AuCl (1.0 mg, 2 mol-%) furnished 3-pyrroline **3a** (39 mg, 71%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.27 (m, 5 H), 5.46 (d, J = 1.5 Hz, 1 H), 4.57 (ABq, J = 12.0 Hz, 2 H), 4.10–4.09 (m, 1 H), 3.88–3.83 (m, 1 H), 3.63 (dd, J = 9.8, 3.5 Hz, 1 H), 3.45 (dd, J = 9.8, 5.8 Hz, 1 H), 1.99 (br s, 1 H), 1.70 (s, 3 H), 0.94 (d, J = 6.8 Hz, 3 H), 0.90 (d, J = 6.8 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.3, 137.6, 128.5, 127.9, 127.7, 125.7, 73.3, 71.2, 70.6, 67.3, 33.7, 19.4, 19.0, 13.7 ppm. IR (neat): $\tilde{\nu}$ = 3365, 3053, 2986 cm^{-1}. HRMS (FAB): calcd. for $C_{16}H_{23}NO$ [M + H]$^+$: m/z = 246.1858; found: m/z = 246.1885.

2-(Benzyloxymethyl)-5-isopropyl-1-methanesulfonyl-3-methyl-2,5-dihydro-1*H*-pyrrole (3b): Conditions A: α-Aminoallene **2b** (52 mg, 0.16 mmol) in CH_2Cl_2 (4 mL) and a solution of $AuCl_3$ in CH_3CN (20 μL, 2 mol-%) furnished 3-pyrroline **3b** (40 mg, 77%, dr = 94:6 by GC and NMR analysis) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.27 (m, 5 H), 5.43*/5.39 (d, J = 1.5 Hz, 1 H), 4.55/4.53* (ABq, J = 12.0 Hz, 2 H), 4.41–4.39*/4.34–4.30 (m, 1 H), 4.38–4.34*/4.24–4.20 (m, 1 H), 4.24*/3.79 (dd, J = 11.0, 2.2 Hz, 1 H), 3.63/3.52* (dd, J = 11.0, 2.0 Hz, 1 H), 2.92*/2.79 (s, 3 H), 2.63–2.55*/2.02–1.94 (m, 1 H), 1.81/1.67* (d, J = 0.8 Hz, 3 H), 0.95/0.90* (d, J = 7.3 Hz, 3 H), 0.82/0.78* (d, J = 6.8 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.6*, 136.3*, 128.6*, 128.5, 128.1*, 128.0*, 127.9, 121.8, 121.1*, 73.7, 73.2*, 73.4, 71.9*, 72.8, 70.8*, 69.1, 66.3*, 39.3*, 35.3, 33.2, 31.1*, 19.5*, 17.0, 15.1*, 14.7, 13.6* ppm. IR (neat): $\tilde{\nu}$ = 3054, 2985 cm^{-1}. HRMS (FAB): calcd. for $C_{17}H_{25}NO_3S$ [M + H]$^+$: m/z = 324.1633; found: m/z = 324.1605.

2-(Benzyloxymethyl)-5-isopropyl-3-methyl-1-(4-tolylsulfonyl)-2,5-dihydro-1*H*-pyrrole (3c): Conditions A: α-Aminoallene **2c** (58 mg, 0.15 mmol) in CH_2Cl_2 (4 mL) and a solution of $AuCl_3$ in CH_3CN (18 μL, 2 mol-%) furnished 3-pyrroline **3c** (54 mg, 93%, dr = 95:5 by GC and NMR analysis) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.75*/7.68 (d, J = 8.3 Hz, 2 H), 7.35–7.10 (m, 7 H), 5.37*/5.19 (d, J = 1.5 Hz, 1 H), 4.52–4.49 (m, 1 H), 4.48–4.44 (m, 1 H), 4.56 (s, 2 H)/4.17* (ABq, J = 12.0 Hz, 2 H), 4.01*/3.92 (dd, J = 10.6, 2.8 Hz, 1 H), 3.65/3.55* (dd, J = 10.6, 2.0 Hz, 1 H), 2.73–2.67*/2.14–2.07 (m, 1 H), 2.41*/2.33 (s, 3 H), 1.67/1.66* (s, 3 H), 0.95/0.90* (d, J = 7.0 Hz, 3 H), 0.82/0.64* (d, J = 6.5 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.6*, 139.4*, 138.4, 138.2*, 136.5*, 129.7, 129.3*, 128.5, 128.3*, 127.8, 127.6*, 127.8, 127.5*, 126.8*, 121.1, 120.9*, 74.4, 72.8*, 73.5, 72.6*, 70.4*, 67.4*, 33.3, 30.7*, 21.7, 21.5*, 19.6*, 16.9, 15.2*, 14.6, 13.8* ppm. IR (neat): $\tilde{\nu}$ = 3054, 2985 cm^{-1}. HRMS (FAB): calcd. for $C_{23}H_{29}NO_3S$ [M + H]$^+$: m/z = 400.1946; found: m/z = 400.1936.

1-[2-(Benzyloxymethyl)-5-isopropyl-3-methyl-2,5-dihydro-2*H*-pyrrol-1(5*H*)-yl]ethanone (3d): Conditions A: α-Aminoallene **2d** (56 mg, 0.19 mmol) in CH_2Cl_2 (4 mL) and a solution of $AuCl_3$ in CH_3CN (24 μL, 2 mol-%) furnished 3-pyrroline **3d** (45 mg, 80%, dr = 70:30 by GC and NMR analysis) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34–7.22 (m, 5 H), 5.43/5.38* (d, J = 1.2 Hz, 1 H), 4.68–4.63/4.55–4.50* (m, 1 H), 4.49* (ABq, J = 12.3 Hz, 2 H)/4.49 (s, 2 H), 4.49–4.45*/4.40–4.35 (m, 1 H), 4.24/3.59* (dd, J = 10.0, 3.0 Hz, 2 H), 2.90–2.82/2.22–2.15* (m, 1 H), 2.06*/2.00 (s, 3 H), 1.78/1.74* (s, 3 H), 0.93*/0.89 (d, J = 7.0 Hz, 3 H), 0.67*/0.56 (d, J = 6.8 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.7*, 169.3, 138.7*, 137.9*, 137.8, 136.4, 128.6*, 128.4*, 128.0, 127.8, 127.6*, 127.6, 121.7, 119.8*, 73.4, 73.2*, 70.9, 70.1*, 70.0, 68.6, 68.1*, 65.8*, 32.0*, 26.5, 22.9*, 19.5, 19.4*, 15.0, 14.8*, 14.2, 13.9* ppm. IR (neat): $\tilde{\nu}$ = 3053, 2985, 1628 cm^{-1}. HRMS (FAB): calcd. for $C_{18}H_{25}NO_2$ [M + H]$^+$: m/z = 288.1964; found: m/z = 288.1935.

***tert*-Butyl 2-(Benzyloxymethyl)-5-isopropyl-3-methyl-2*H*-pyrrole-1(5*H*)-carboxylate (3e):** Conditions A: α-Aminoallene **2e** (48 mg, 0.14 mmol) in CH_2Cl_2 (4 mL) and a solution of $AuCl_3$ in CH_3CN (17 μL, 2 mol-%) furnished 3-pyrroline **3e** (33 mg, 69%, dr = 46:54 by GC and NMR analysis) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.24 (m, 10 H), 5.40 (d, J = 1.2 Hz, 1 H), 5.36 (d, J = 1.3 Hz, 1 H), 4.55 (ABq, J = 12.3 Hz, 2 H), 4.50 (s, 2 H), 4.49–4.46 (m, 1 H), 4.40–4.35 (m, 1 H), 4.34–4.31 (m, 1 H), 4.28–4.25 (m, 1 H), 4.16 (dd, J = 10.0, 3,2 Hz, 1 H), 3.83 (dd, J = 10.0, 4.0 Hz, 1 H), 3.65–3.59 (m, 2 H), 2.82–2.74 (m, 1 H), 2.53–2.45 (m, 1 H), 1.75 (s, 3 H), 1.74 (s, 3 H), 1.50 (s, 9 H), 1.41 (s, 9 H), 0.89 (d, J = 7.0 Hz, 3 H), 0.88 (d, J = 7.0 Hz, 3 H), 0.64 (d, J = 6.8 Hz, 3 H), 0.62 (d, J = 6.8 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.9, 153.3, 138.9, 138.5, 137.2, 137.1, 128.5, 128.4, 127.7, 127.6, 127.5, 121.1, 120.8, 79.3, 79.2, 73.5, 73.3, 69.6, 69.3, 68.9, 67.9, 67.6, 66.6, 29.8, 28.7, 27.5, 27.0, 19.5, 19.3, 15.1, 15.0, 14.2, 14.0 ppm. IR (neat): $\tilde{\nu}$ = 3054, 2985, 1744 cm^{-1}. HRMS (FAB): calcd. for $C_{21}H_{31}NO_3$ [M + H]$^+$: m/z = 346.2382; found: m/z = 346.2366.

2-(*tert*-Butyldimethylsilyloxymethyl)-5-hexyl-3-methyl-2,5-dihydro-1*H*-pyrrole (3f): Conditions A: α-Aminoallene **2f** (50 mg, 0.16 mmol) in CH_2Cl_2 (4 mL) and a solution of $AuCl_3$ in CH_3CN (20 μL, 2 mol-%) furnished 3-pyrroline **3f** (41 mg, 82%, dr = 85:15 by GC and NMR analysis) as a colorless oil. Conditions B-1: α-Aminoallene **2f** (70 mg, 0.23 mmol) in CH_2Cl_2 (7 mL) and AuCl (1.0 mg, 2 mol-%) furnished 3-pyrroline **3f** (43 mg, 61%, dr = 85:15 by GC and NMR analysis) as a colorless oil. Conditions B-2: α-Aminoallene **2f** (50 mg, 0.16 mmol) in CH_2Cl_2 (5 mL) and AuI (1.0 mg, 2 mol-%) furnished 3-pyrroline **3f** (38 mg, 76%, dr = 85:15 by GC and NMR analysis) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.51/5.43* (br s, 1 H), 4.08–4.00 (m, 2 H), 3.85/3.82* (dd, J = 10.6, 3.7 Hz, 1 H), 3.72/3.65* (dd, J = 10.6, 4.3 Hz, 1 H), 1.71 (s, 3 H), 1.62–1.52 (m, 2 H), 1.39–1.25 (m, 8 H), 0.90–0.85 (m, 3 H), 0.87 (s, 9 H), 0.07, 0.05 (2 × s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.1*, 136.9, 126.9*, 125.9, 68.6*, 64.6*, 63.4*, 31.9*, 31.8, 29.4*, 29.3, 26.6*, 26.4, 26.0*, 22.8*, 22.7, 18.4, 18.3*, 14.2*, 14.1, 13.7*, 13.4, –5.2*, –5.4* ppm. IR (neat): $\tilde{\nu}$ = 3365, 3052, 2956 cm^{-1}. HRMS (FAB): calcd. for $C_{18}H_{37}NOSi$ [M + H]$^+$: m/z = 312.2723; found: m/z = 312.2741.

2-(Benzyloxymethyl)-3,5-dimethyl-2,5-dihydro-1*H*-pyrrole (3g): Conditions A: α-Aminoallene **2g** (48 mg, 0.23 mmol) in CH_2Cl_2 (5 mL) and a solution of $AuCl_3$ in CH_3CN (30 μL, 2 mol-%) furnished 3-pyrroline **3g** (34 mg, 71%, dr = 90:10 by GC and NMR analysis) as a colorless oil. Conditions B: α-Aminoallene **2g** (48 mg, 0.23 mmol) in CH_2Cl_2 (5 mL) and AuCl (1.0 mg, 2 mol-%) fur-

nished 3-pyrroline **3g** (29 mg, 60%, *dr* = 90:10 by GC and NMR analysis) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.27 (m, 5 H), 5.40*/5.34 (br s, 1 H), 4.59 (ABq, *J* = 11.8 Hz, 2 H), 4.40–4.32 (m, 1 H), 4.30–4.26*/4.22–4.18 (m, 1 H), 3.71 (dd, *J* = 10.0, 3.3 Hz, 1 H), 3.54 (dd, *J* = 10.0, 5.3 Hz, 1 H), 1.69 (s, 3 H), 1.41/1.36* (d, *J* = 6.6 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.0*, 135.8*, 135.6, 128.5*, 128.1, 128.0, 128.0*, 127.8*, 127.7*, 73.4*, 73.3, 69.1*, 66.9*, 62.4, 60.4*, 20.8, 20.5*, 13.4*, 13.2 ppm. IR (neat): $\tilde{\nu}$ = 3317, 3170, 3031, 2861 cm^{-1}. HRMS (FAB): calcd. for $C_{14}H_{19}NO$ [M + H]$^+$: *m*/*z* = 218.1545; found: *m*/*z* = 218.1574.

2-(*tert*-Butyldimethylsilyloxymethyl)-3-methyl-5-phenyl-2,5-dihydro-1*H*-pyrrole (3h): Conditions A: α-Aminoallene **2h** (45 mg, 0.15 mmol) in CH_2Cl_2 (5 mL) and a solution of $AuCl_3$ in CH_3CN (19 μL, 2 mol-%) furnished 3-pyrroline **3h** (37 mg, 79%) as a colorless oil. Conditions B: α-Aminoallene **2h** (29 mg, 0.10 mmol) in CH_2Cl_2 (3 mL) and AuCl (0.5 mg, 2 mol-%) furnished 3-pyrroline **3h** (20 mg, 69%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30–7.22 (m, 5 H), 5.50 (br s, 1 H), 5.04 (br s, 1 H), 4.05 (br s, 1 H), 3.74 (dd, *J* = 8.0, 3.4 Hz, 1 H), 3.62 (dd, *J* = 8.0, 4.6 Hz, 1 H), 1.81 (s, 3 H), 0.91 (s, 9 H), 0.09 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.2, 139.1, 128.6, 127.8, 127.2, 127.0, 69.5, 67.8, 65.9, 26.0, 18.4, 13.9, –5.2, –5.3 ppm. IR (neat): $\tilde{\nu}$ = 3367, 3061, 2928 cm^{-1}. HRMS (FAB): calcd. for $C_{18}H_{29}NOSi$ [M + H]$^+$: *m*/*z* = 304.2097; found: *m*/*z* = 304.2072.

Treatment of α-Aminoallene 2a with Stoichiometric Amounts of Gold(III) Bromide: $AuBr_3$ (94 mg, 0.22 mmol) was added at –90 °C under argon to a solution of α-aminoallene **2a** (53 mg, 0.22 mmol) in dry THF (10 mL). After the system had been stirred with gradual warming from –90 °C to room temperature overnight, saturated Na_2CO_3 solution was slowly added at 0 °C, and the crude product was extracted with ethyl acetate. The combined organic phases were washed with brine and dried with sodium sulfate, the solvent was removed by rotary evaporation, and the crude product was purified by column chromatography (CH_2Cl_2/MeOH, 10:1) on silica gel to afford a mixture of 2-(benzyloxymethyl)-5-isopropyl-3-methyl-1*H*-pyrrole (**4**, 15 mg) and other unidentified products. The pyrrole **4** was identified by characteristic peaks in the ^{1}H NMR spectrum and by high-resolution mass spectrometry. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.30 (s, 1 H), 4.70 (s, 2 H), 3.48 (s, 2 H). HRMS (FAB): calcd. for $C_{16}H_{21}NO$ [M + H]$^+$: *m*/*z* = 244.1701; found: *m*/*z* = 244.1679.

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