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Gold- and Silver-Catalyzed Tandem Amination/Ring Expansion of Cyclopropyl Methanols with Sulfonamides as an Expedient Route to Pyrrolidines

Weidong Rao and Philip Wai Hong Chan*[a]

Abstract: An efficient synthetic route to pyrrolidines that relies on AuCl/AgOTf-catalyzed tandem amination/ring expansion of substituted cyclopropyl methanols with sulfonamides is reported herein. The reactions proceed rapidly at 100 °C with catalyst loadings as low as 2 mol % and produce the pyrrolidine products in yields of 30–95 %. The method was shown to be applicable to a broad range of cyclopropyl methanols, including unactivated ones, and sulfonamide substrates containing electron-withdrawing, electron-donating, and sterically-demanding substituents. The mechanism is suggested to involve activation of the alcohol substrate by the AuCl/AgOTf catalyst, followed by ionization of the starting material, which causes ring opening of the cyclopropane moiety and trapping by the sulfonamide nucleophile. The resultant aminated acyclic intermediate undergoes subsequent intramolecular hydroamination to give the pyrrolidine.

Keywords: gold · nitrogen heterocycles · ring expansion · silver · synthetic methods

Introduction

Gold complexes have emerged as powerful and versatile Lewis acidic catalysts for stereoselective C–X (X = C, N, O, S) bond formation in recent years.[1–7] Generally, this type of reaction relies on interaction of the gold catalyst with the π bonds of alkenes, alkynes, and allenes. In this regard, the development of new methods that explore the scope of other functional groups in gold-catalyzed reactions has gained momentum. In a recent notable advance Campagne and co-workers showed that propargylation of allylic silanes, arenes, thiols, and alcohols by propargylic alcohols proceeds smoothly in the presence of $HAuCl_4 \cdot 2H_2O$ as catalyst.[2] Following this seminal work, we,[3] Dyker et al.,[4] and Beller et al.[5] reported similar efficient gold-catalyzed approaches for Friedel–Crafts allylic alkylation, propargylation, and benzylation of aromatic compounds with allylic, propargylic, and benzylic alcohols. Aponick and co-workers recently demonstrated that formation of tetrahydropyrans by gold-catalyzed intramolecular cyclization of monoallylic diols could be accomplished in good to excellent yields.[6] A tandem amination/intramolecular hydroamination strategy for the synthesis of pyrroles from 1-en-4-yn-3-ols mediated by $HAuCl_4 \cdot 4H_2O$ and $AuCl_3$-catalyzed allylic alkylation of sulfonamides with allylic alcohols were recently communicated by Liang et al.[7] and Liu et al.[8] In view of these works and our ongoing program on carbon–nitrogen bond formation,[9] we turned our attention to expanding the scope of alcohols as pre-electrophiles in gold catalysis as the basis for developing new strategies for constructing pyrrolidines.

The pyrrolidine ring motif is a common structural unit found in a myriad of bioactive natural products and pharmaceutically interesting compounds.[10–15] These include anatoxin,[11] hyacinthacine C_1,[12] (−)-kainic acid,[13] oxazolomycin A,[14] and (+)-preussin (Scheme 1),[15] which are reported to exhibit bioactivities ranging from antiviral to cytotoxic. Hence, developing methods for efficient formation of this saturated nitrogen-containing heterocycle is of immense importance in organic synthesis. Recently, Krause et al.[16] and He et al.[17] respectively described gold-catalyzed cycloisomerization of α-amino allenes and intra- and intermolecular hydroamination of alkenes as mild, efficient, and atom-economic strategies[18] for pyrrolidine ring synthesis. Following these works, Shi et al.[19] and Togni et al.[20] independently reported that tandem versions of gold-catalyzed hydroaminations involving reactions of methylene cyclopropanes (MCPs) or vinyl cyclopropanes (VCPs) with sulfonamides

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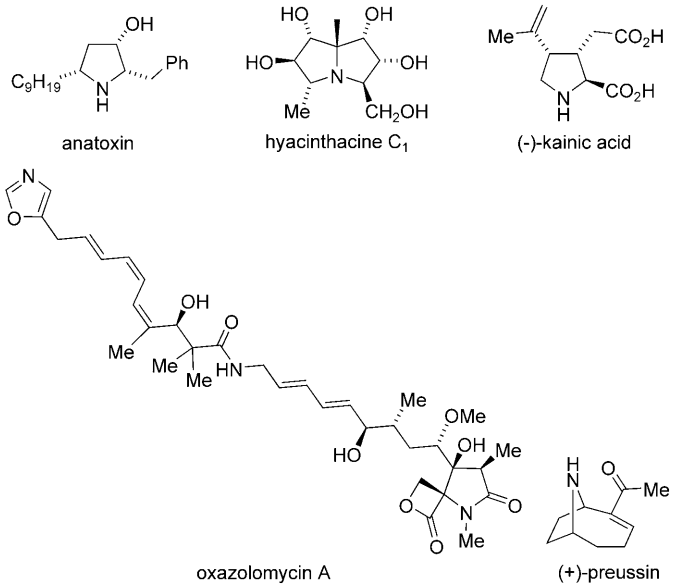
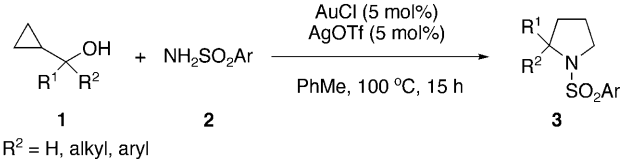


Scheme 1. Examples of bioactive compounds containing a pyrrolidine moiety.

are also efficient preparative methods. A synthetic approach that also relies on the exceptional activity and mild conditions offered by homogenous gold catalysis but makes use of substituted cyclopropyl methanols as starting materials, on the other hand, is not known. Although Pd-catalyzed intramolecular aminocyclization of amino-tethered allylic alcohols has been described,[21,22] the reactions usually require relatively high catalyst loadings and additives. In addition, limited examples demonstrating substrate scope and moderate to good regio- and chemoselectivities have lessened their utility in organic synthesis. In this regard, we envisioned that a gold-catalyzed strategy involving the use of substituted cyclopropyl methanols as pre-electrophiles would be attractive from a synthetic standpoint, as the ease of preparing the alcohol starting material provides the possibility to introduce a wide variety of substituents and the potential to form a quaternary carbon center by addition to a tertiary alcohol. Moreover, H_2O is potentially the only side product. Herein we report a convenient synthetic route to pyrrolidine derivatives that involves tandem amination/ring expansion of substituted cyclopropyl methanols and sulfonamides catalyzed by AuCl in the presence of AgOTf (OTf = trifluoromethanesulfonate) as cocatalyst (Scheme 2). The reaction proceeds in good to excellent yields of up to 95% for a wide variety of readily available starting materials. A



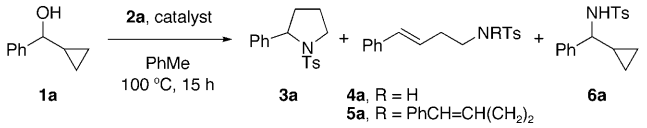
Scheme 2. Gold- and silver-catalyzed tandem amination/ring expansion of cyclopropyl methanols with sulfonamides.

study that delineates the possible mechanism of the AuCl/AgOTf-catalyzed pyrrolidine formation process is also presented.

Results and Discussion

Catalyst screening: We chose cyclopropyl(phenyl)methanol (**1a**) and toluene-4-sulfonamide (**2a**) as model substrates to establish the reaction conditions (Table 1). The best result was obtained by treatment of 1 equiv of **1a** and 2 equiv of **2a** with 5 mol% of AuCl and 5 mol% of AgOTf in toluene at 100°C for 15 h, which furnished **3a** as the sole product in 95% yield (Table 1, entry 1). The pyrrolidine product was confirmed by ^{1}H NMR analysis and X-ray crystal structure determination of a closely related product (see below). Notably, a slightly lower yield of 91% could be obtained on lowering the catalyst loading of both AuCl and AgOTf to 2 mol% (Table 1, entry 2). In contrast, performing the reaction in other solvents gave **3a** in markedly lower yields and with a variety of side products. Use of chlorinated solvents such as $CHCl_3$ and 1,2-dichloroethane afforded either (*E*)-4-methyl-*N*-(4-phenylbut-3-enyl)benzenesulfonamide (**4a**) as the major product in 44% yield or 4-methyl-*N*,*N*-bis[(*E*)-4-phenylbut-3-enyl]benzenesulfonamide (**5a**) in a trace amount (Table 1, entries 3 and 4). On the other hand, when

Table 1. Optimization of reaction conditions.[a]



Entry	Catalyst	Solvent	Yield [%][b]			
			3a	**4a**	**5a**	**6a**
1	AuCl/AgOTf	PhMe	95	–	–	–
2[c]	AuCl/AgOTf	PhMe	91	–	3	–
3	AuCl/AgOTf	$CHCl_3$	40	44	–	–
4	AuCl/AgOTf	$(CH_2Cl)_2$	67	–	–[d]	–
5	AuCl/AgOTf	MeCN	–	–	–	33
6	AuCl/AgOTf	THF	–	-	–	–
7	Ph_3PAuCl/AgOTf	PhMe	80	–	2	–
8	$Ph_3PAuCl/AgSbF_6$	PhMe	42	40	–[d]	–
9	$AuCl_3$/AgOTf	PhMe	72	10	–[d]	–
10	AuCl	PhMe	–	–	–	–
11	$AuCl_3$	PhMe	–	–	–	15
12	AgOTf	PhMe	–	–	–	80
13	$FeCl_3.6H_2O$	PhMe	–	–	–	21
14	$Yb(OTf)_3$	PhMe	–	22	–	55
15	$Cu(OTf)_2$	PhMe	83	–	–[d]	–
16	$InCl_3$	PhMe	–	–	–	–
17	$ZnCl_2$	PhMe	–	–	–	–
18	$BF_3{\cdot}Et_2O$	PhMe	–	66	3	–
19[e]	TfOH	PhMe	71	–[d]	2	–
20	TfOH	PhMe	87	–	–	–
21	*p*-TsOH·H_2O	PhMe	–	28	–	–
22	TFA	PhMe	–	–	–	29

[a] All reactions were performed at 100°C for 15 h with catalyst:**1a**:**2a** ratio of 1:20:40. [b] Yields of isolated products. [c] Reaction conducted with a catalyst loading of 2 mol%. [d] Trace amount: <1% of compound isolated after flash column chromatography. [e] Reaction conducted with TfOH catalyst loading of 20 mol%.

the solvent was changed to MeCN, *N*-[cyclopropyl-(phenyl)methyl]-4-methylbenzenesulfonamide (**6a**) was preferentially obtained as the sole product in 33% yield, while the use of THF as solvent resulted in a mixture of side products that could not be identified by ^{1}H NMR analysis (Table 1, entries 5 and 6). The structure of **6a** was confirmed by ^{1}H NMR analysis and X-ray crystal analysis of a closely related product (see below).

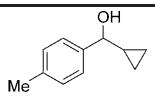
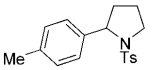
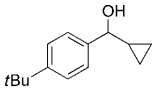
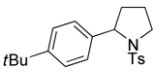
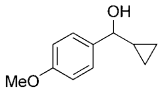
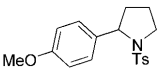
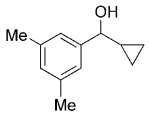
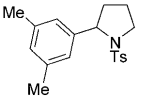
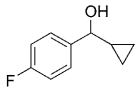
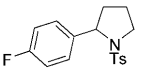
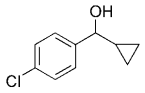
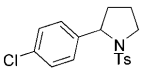
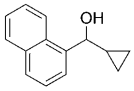
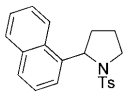
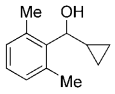
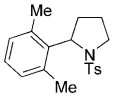
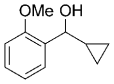
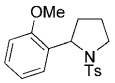
Inspection of entries 7–22 in Table 1 reveals that tandem amination/ring expansion of **1a** with **2a** in the presence of other Lewis and Brønsted acids as catalyst are less effective. When Ph_3PAuCl was used in combination with AgOTf or $AgSbF_6$, or $AuCl_3$ with AgOTf, lower product yields of 42–80% were obtained (Table 1, entries 7–9). Moreover, in these reactions the use of Ph_3PAuCl and AgOTf resulted in formation of **4a** as a side product while those mediated by $Ph_3PAuCl/AgSbF_6$ or $AuCl_3$/AgOTf gave both **4a** (10–40%) and **5a** (2% or less) as side products. A similar outcome was found when reactions employing single Lewis acidic catalysts such as AuCl, $AuCl_3$, AgOTf, $Cu(OTf)_2$, $FeCl_3{\cdot}6H_2O$, $InCl_3$, $Yb(OTf)_3$, and $ZnCl_2$ were examined. In our hands, reaction with $Cu(OTf)_2$ as catalyst afforded **3a** in a lower yield of 83% and a trace amount of **5a** (Table 1, entry 15). However, the analogous reactions mediated by $AuCl_3$, AgOTf, $FeCl_3{\cdot}6H_2O$, and $Yb(OTf)_3$ were found to preferentially furnished **6a** in 15–80% yield along with a variety of byproducts that could not be identified by ^{1}H NMR measurements; **4a** was also afforded in 22% yield with $Yb(OTf)_3$ as catalyst (Table 1, entries 11–14). A switch in chemoselectivity was further observed on employing $BF_3{\cdot}Et_2O$, which afforded **4a** and **5a** in yields of 66 and 3%, respectively (Table 1, entry 18). In marked contrast, no reaction was found on changing the catalyst to AuCl, $InCl_3$, or $ZnCl_2$ (Table 1, entries 10, 16, and 17).

We also examined the Brønsted acid catalysts trifluoromethanesulfonic acid (TfOH), *para*-toluenesulfonic acid monohydrate (*p*-TsOH·H_2O), and trifluoroacetic acid (TFA) (Table 1, entries 19–22). The reaction of **1a** with **2a** in the presence of 5 mol% of TfOH as catalyst was the only case in which the desired product **3a** was furnished in 71% yield along with a trace amount of **4a** and **5a** (2% yield, Table 1, entry 19). Efficient transformation to the product in 87% yield was only achieved when the reaction was repeated with an increased catalyst loading of 20 mol% of TfOH catalyst (Table 1, entry 20). Based on recent results of He et al. and our earlier findings for the analogous AgOTf-catalyzed reaction (entry 12 in Table 1), this and the significantly lower concentration of TfOH in 5 mol% of AuCl/AgOTf also provides evidence that the cationic gold(I) complex is the active species.[23] In contrast to the activity exhibited by TfOH, when *p*-TsOH·H_2O was employed as catalyst, the reaction was found to give **4a** exclusively in 28% yield, while **6a** was the only product in 29% yield on changing the catalyst to TFA (Table 1, entries 21 and 22). In each of these reactions, a wide variety of side products was also obtained which could not be separated by flash column chromatography or identified by ^{1}H NMR analysis of the crude mixtures.

Variation of the substituted cyclopropyl methanol electrophile: To investigate the scope of the AuCl/AgOTf-catalyzed tandem amination/ring-expansion reaction, we applied these conditions to a series of substituted cyclopropyl methanols (Table 2). Reactions of substituted cyclopropyl methanols containing a pendant electron-donating group with **2a** afforded the corresponding pyrrolidine compounds **3b,c** and **3e** in yields of 81–91% (Table 2, entries 1, 2, and 4). Similarly, analogous reactions of **1f,g** containing electron-withdrawing groups with **2a** afforded the corresponding pyrrolidine products **3f,g** in comparable yields of 77–84% (Table 2, entries 5 and 6). Substituted cyclopropyl methanols **1h,i** bearing a sterically bulky naphthyl or 2,6-dimethylbenzene group, respectively, were found to be good alcoholic substrates affording good product yields (Table 2, entries 7 and 8). Similarly, tertiary substituted cyclopropyl methanols **1k,l** gave the corresponding quaternary substituted pyrrolidines **3k,l** in 60–68% yield (Table 2, entries 10 and 11). More notably, **3m–o** could be obtained in moderate to good yields from the respective reactions of **1o–q** with **2a** (Table 2, entries 14–16). Although a slightly higher catalyst loading of 10 mol% was required, this demonstrated that the present method is also suitable for unactivated alkyl-substituted cyclopropyl methanols. On the other hand, extreme steric effects of tertiary substituted cyclopropyl methanols may play a role, since two bulky geminal groups, such as two benzene rings, led to preferential provided acyclic but-3-enylsulfonamide **4b** in 81% yield (Table 2, entry 12). Strongly electron donating pendant groups such as alkynyl and methoxyphenyl on the alcohol substrate also detrimentally influenced the carbon–nitrogen bond-forming process. As shown in entries 3 and 9 in Table 2, both **3d** and **3j**, which was also structurally characterized by X-ray crystal analysis (Figure 1),[24] were obtained in comparable low yields regardless of whether the electron-rich starting alcohol contained a sterically bulky group or not. Similarly, reaction of alkyne **1n** with **2a** was found to result in formation of acyclic enyne **4c** as the sole product in 69% yield with a *cis*:*trans* ratio of 1:1 (Table 2, entry 13).[25] Retardation of reaction by a strongly electron-donating substituent on the substrate has also been reported by Shi et al.[19] and Hartwig et al.[26] in their approaches to pyrrolidines.

Variation of the nitrogen nucleophile: To further explore the scope of the AuCl/AgOTf-catalyzed reactions, the tandem amidation/ring expansion of **1a** with a variety of different nitrogen nucleophiles was examined (Table 3). Under the standard conditions, reaction of **1a** with benzenesulfonamide (**2b**) gave **3p** in 84% yield (Table 3, entry 1), and 4-bromobenzenesulfonamide (**2c**) gave the corresponding pyrrolidine product **3q** in 68% yield (Table 3, entry 2). In contrast, a markedly lower product yield was obtained when *para*-nitro-substituted sulfonamide **2d** was employed as nucleophile, presumably due its significantly lower nucleophilicity (Table 3, entry 3). On the other hand, the use of a more nucleophilic sulfonamide such as **2e**, which contains a *para*-methoxyphenyl group, was found to result in no reac-

Table 2. AuCl/AgOTf-catalyzed tandem amination/ring expansion of **1b–q** with **2a**.[a]

Entry	Alcohol		Product		Yield [%][b]
1		**1b**		**3b**	81
2		**1c**		**3c**	91
3		**1d**		**3d**	30
4		**1e**		**3e**	89
5		**1f**		**3f**	84
6		**1g**		**3g**	77
7		**1h**		**3h**	80
8		**1i**		**3i**	70
9		**1j**		**3j**	34
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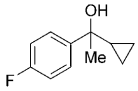
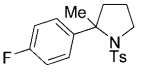
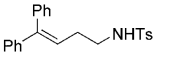
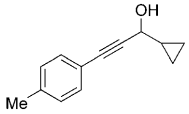
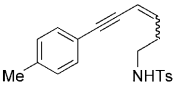
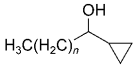
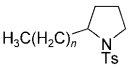
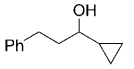
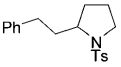
11		**1l**		**3l**	68
12		**1m**		**4b**	81
13		**1n**		**4c**	69[d]
14[c]		**1o,p**		**3m**, $n=7$	50
15[c]				**3n**, $n=11$	37
16[c]		**1q**		**3o**	44

[a] All reactions were performed at 100 °C in toluene for 15 h with AuCl/AgOTf: **1**: **2a** ratio = 1: 20: 40. [b] Yields of isolated products. [c] Reaction conducted with 10 mol % AuCl/AgOTf catalyst. [d] Isolated as a mixture of *trans* and *cis* isomers in 1:1 ratio.

tion on the basis of both TLC and ^{1}H NMR analysis (Table 3, entry 4). In addition, the analogous reactions of **1a** with carbamates such as **2f**,**g** did not proceed as anticipated. Under our experimental conditions, these reactions were found to afford amidated cyclopropanes **6b**,**c** as the sole adducts in 85 and 73 % yield, respectively (Table 3, entries 5 and 6). In both cases, formation of the desired pyrrolidine adduct could not be detected by ^{1}H NMR analysis on increasing the catalyst loading to 10 mol % or increasing the reaction time to 36 h.

On the mechanism of the tandem amidation/ring expansion of substituted cyclopropyl methanols with sulfonamides: Competitive formation of **4a** and **6a** under certain conditions during the reactions of **1a** with **2a** outlined in Table 1 led us to initially speculate on their possible involvement as intermediates in the present AuCl/AgOTf-catalyzed procedure. To support this hypothesis and gain a better understanding of the reaction mechanism, we conducted the following experiments using **1a** and **2a** as probe substrates. Treatment of these starting materials with 5 mol % of AuCl and AgOTf in toluene for 15 h at room temperature cleanly gave **6a** as the only product in 95 % yield (Table 4, entry 1). Under these modified conditions, reactions of **2a** with cyclopropyl methanols bearing electron-withdrawing, electron-donating, and sterically demanding substituents also proceeded in a similar manner at room temperature to give the corresponding substituted cyclopropyl sulfonamides **6d–h** in yields of 61–99 % (Table 4, entries 2–6). The structure of **6h** was established by X-ray crystallography (Figure 2).[24] Development of a convenient route to compounds having both cyclopropane and sulfonamide functionality is noteworthy, as these pharmacophores may have interesting bioactivity. On the other hand, **4a** was exclusively furnished in 93 % yield by the analogous AuCl/AgOTf-catalyzed reaction of **1a** and **2a** at 100 °C for 1 h. In both instances, conversion to **3a** from **4a** in 93 % yield and from **6a** in 70 % yield was found on re-treating these compounds under the standard conditions of 5 mol % of AuCl and AgOTf in toluene at 100 °C

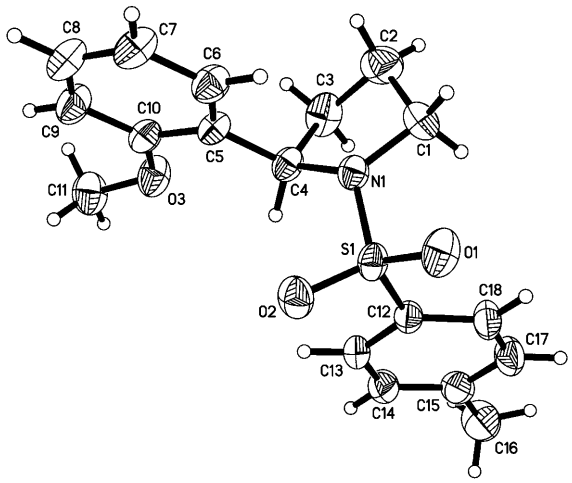
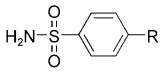


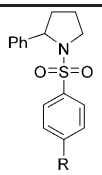
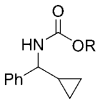
Figure 1. ORTEP drawing of **3j** with thermal ellipsoids at 50% probability.[24]

Table 3. AuCl/AgOTf-catalyzed tandem amination/ring expansions of **1a** with **2b–g**.[a]



2b, R = H
2c, R = Br
2d, R = NO_2
2e, R = OMe

2f, R = *t*Bu
2g, R = Bn

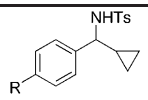
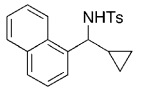
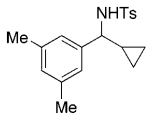
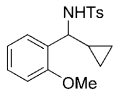
Entry	Nucleophile	Product		Yield [%][b]
1	**2b**		**3p**, R = H	84
2	**2c**		**3q**, R = Br	68
3	**2d**		**3r**, R = NO_2	31
4	**2e**			–[c]
5	**2f**		**6b**, R = *t*Bu	85
6	**2g**		**6c**, R = Bn	73

[a] All reactions were performed at 100 °C in toluene for 24 h with AuCl/AgOTf:**1a**:**2** ratio of 1:20:40. [b] Yields of isolated products. [c] No reaction.

for 15 h.[27] In the latter case, monitoring the reaction by ^{1}H NMR spectroscopy revealed complete conversion of **6a** to a mixture of **3a** and **4a** in a ratio of 1:2 after 1 h. This suggested a pathway by which generation of an intermediate that closely resembles **4** could precede product formation. The possible involvement of such a species would also account for our findings on the reaction of enantiopure **1a** with **2a**. Under our experimental conditions, pyrrolidine adduct **3a** was obtained as a racemic mixture in 93% yield, as shown in Scheme 3.[28]

On the basis of the above results, we tentatively propose the present AuCl/AgOTf-catalyzed pyrrolidine-forming reaction to proceed by the mechanism outlined in Scheme 4, although it is highly speculative. In a manner similar to that put forward by us,[3] Campagne et al.[2] and Aponick et al.,[6]

Table 4. AuCl/AgOTf-catalyzed amination of **1a-j** with **2a**.[a]

Entry	Alcohol	Product		Yield [%][b]
1	**1a**		**6a**, R = H	95
2	**1d**		**6d**, R = OMe	95
3	**1f**		**6e**, R = F	87
4	**1h**		**6f**	91
5	**1i**		**6g**	61
6	**1j**		**6h**	99

[a] All reactions were performed at room temperature in toluene for 15 h with AuCl/AgOTf:**1a**:**2** ratio of 1:20:40. [b] Yields of isolated products.

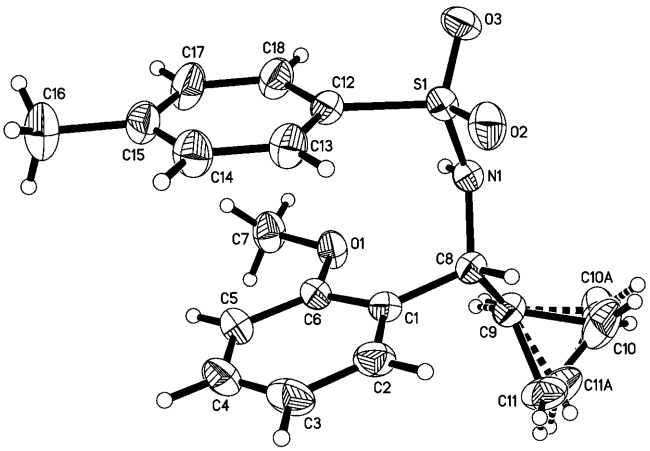
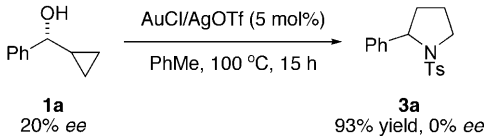


Figure 2. ORTEP drawing of **6h** with thermal ellipsoids at 50% probability.[24]

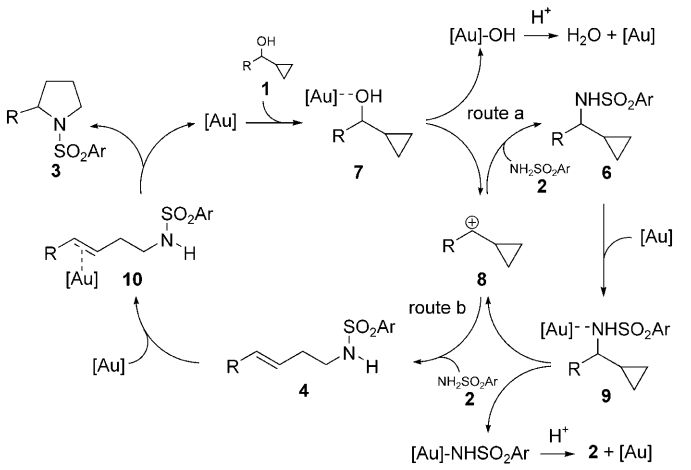


1a
20% *ee*

3a
93% yield, 0% *ee*

Scheme 3. AuCl/AgOTf-catalyzed tandem amination/ring expansion of enantiopure **1a** with **2a**.

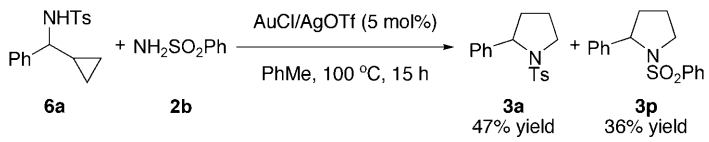
we postulate that the gold/silver catalyst combination activates alcohol substrate **1** by coordinating to the oxygen atom. This affords gold(I)-coordinated cyclopropyl methanol **7**, which can undergo elimination to give carbocation intermediate **8** and [Au]-OH, which releases the gold catalyst by protodemetalation. It is possible that this newly formed cationic species could initially react with **2** to produce cyclopropyl sulfonamide **6** (route a in Scheme 4). However, as the introduced sulfonamide functionality can also be activated by coordination to the catalyst, the C–N bond-forming step may be reversible, and the carbocation intermediate is reformed as quickly as it is amidated. Alternatively, as



Scheme 4. Tentative mechanism for AuCl/AgOTf-catalyzed tandem amination/ring expansion of substituted cyclopropyl methanols with sulfonamides.

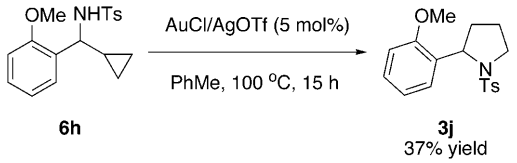
shown in route b in Scheme 4, the amidation step could be skipped altogether, and ring opening of the cyclopropane moiety of **8** followed by trapping with **2** directly furnishes acyclic sulfonamide **4**. Subsequent coordination to the catalyst might be expected to give the gold(I)-activated alkene species **10**, which is the active species that undergoes intramolecular hydroamination to afford the pyrrolidine product. A similar cyclization step was proposed by Shi and co-workers for the gold(I)-catalyzed tandem ring-opening/ring-closing hydroamination of MCPs.[19]

Although a number of pathways are conceivable, we surmise that the mechanism of the present procedure to likely to proceed via ring-opening of the cyclopropane moiety of **8** irrespective of whether the reaction follows routes a and b or only route b in Scheme 4. This is supported by our isolating **3a** and **3p** in yields of 47 and 36%, respectively, from the crossover reaction of 1 equiv of **6a** with 1 equiv of **2b** in the presence of 5 mol% of AuCl/AgOTf under the conditions described in Scheme 5. A similar outcome was also obtained on repeating the reaction with 5 mol% of TfOH as catalyst, which furnished **3a** and **3p** in yields of 42 and 31%, respectively. The origin of the *N*,*N*-substituted sulfonamide side product **5** could be due to the acyclic adduct **4** competing with **2** in trapping the species resulting from fragmentation of **8**. More notably, the manner in which the catalyst can efficiently coordinate to the alcohol substrate and resultant intermediates formed during the tandem C–N bond-forming process proposed in Scheme 4 seems to be a pivotal aspect of the present procedure. This is evident in a



Scheme 5. AuCl/AgOTf-catalyzed ring expansion of **6a** with **2b**.

number of experiments examined in this work. First, the role of AgOTf in producing a more electrophilic gold catalyst that can participate in substrate coordination seems to be crucial for the reaction to proceed smoothly, since neither AgOTf nor AuCl was found to be an effective catalyst. Moreover, the outcome of the reaction is influenced by the nature of the solvent: polar solvents such as $CHCl_3$, 1,2-dichloroethane, MeCN, and THF have a detrimental effect on both product yields and chemoselectivity. This also appears to be operative when such interactions are presumably weakened due to competitive coordination with a very electron rich neighbor on the alcohol substrate or nitrogen nucleophile, such as a methoxyphenyl or alkyne moiety, as in **1d**, **1j**, **1n**, and **2e**. We found that in each of these cases, either markedly lower product yields or the acyclic enyne adduct were obtained or no reaction could be detected. Indeed, this is further supported by the fact that when a solution of toluene containing **6h** was treated with 5 mol% of AuCl/AgOTf at 100°C for 15 h, the expected pyrrolidine **3j** was obtained in a yield of 37%, comparable to those found for the analogous reactions of **1d** and **1j** (Scheme 6).



Scheme 6. AuCl/AgOTf-catalyzed ring expansion of **6h**.

Conclusion

We have described an efficient AuCl/AgOTf-catalyzed strategy for formation of pyrrolidine derivatives, including examples with quaternary centers, starting from substituted cyclopropyl methanols. The method is applicable to a wide range of activated and unactivated substituted cyclopropyl methanol and sulfonamide substrates containing electron-withdrawing, electron-donating, and sterically-demanding substituents. In addition, the gold-catalyzed tandem reaction exhibits excellent catalytic activity at low catalyst loadings. When the reactions were conducted at room temperature, *N*-cyclopropylmethyl sulfonamides with potentially interesting bioactivity were formed chemoselectively. Our studies suggest activation of the substituted cyclopropyl methanol substrate by the gold catalyst, which leads to ionization of the alcohol. This possibly triggers subsequent ring opening of the cyclopropane moiety followed by trapping with the sulfonamide nucleophile to give an acyclic aminated intermediate that undergoes intramolecular hydroamination to form the pyrrolidine product. Our studies revealed that TfOH can also mediate the tandem amidation/ring expansion process, but the lower product yields and selectivities exhibited by TfOH along with the significantly milder conditions of gold catalysis provides an attractive alternative synthetic approach for the formation of pyrrolidines. While the

findings of this study suggest it is unlikely that TfOH potentially generated in situ is the true species promoting the reaction, it also demonstrates the care required when interpreting such results, given the similar reactivities exhibited by both gold and Brønsted acid catalysts.

Experimental Section

General remarks: All reactions were performed under an argon atmosphere. Unless otherwise specified, all reagents and starting materials were purchased from commercial sources and used as received. All substituted cyclopropyl methanol substrates used in this work were prepared by following literature procedures.[29] Solvents were purified by standard literature procedures; CH_2Cl_2 was purified prior to use by passing through a PURESOLV Solvent Purification System. Analytical TLC was performed on Merck 60 F254 precoated silica gel plates. Visualization was achieved with UV light (254 nm). Flash chromatography was performed on Merck silica gel 60 with a solvent-gradient system (EtOAc:*n*-hexane as eluent). ^{1}H and ^{13}C NMR spectra were measured on a Bruker Avance 400 MHz spectrometer. Chemical shifts (ppm) were recorded with tetramethylsilane (TMS) as internal reference. Infrared spectra were recorded on Shimadzu IR Prestige-21 FTIR Spectrometer. Solid samples were examined as a thin film between NaCl plates. Low-resolution mass spectra were determined on a Finnigan LCQ XP MAX mass spectrometer. High-resolution mass spectra (HRMS) were obtained on a Finnigan MAT95XP LC/HRMS mass spectrometer.

General procedure for optimizing the Lewis and Brønsted acid-catalyzed tandem amination/ring expansion of 1a with 2a: For reactions with a gold/silver catalyst combination, the gold (15 μmol) and silver (15 μmol) catalysts were first stirred in toluene (1.5 mL) at room temperature for 1 h. In all other cases, the catalyst was added to a toluene solution prior to adding the starting materials. Then a toluene solution (1.5 mL) containing **1a** (0.3 mmol) and **2a** (0.6 mmol) was added, and the reaction mixture stirred at 100 °C and monitored to completion by TLC analysis. The reaction mixture was then cooled and the solvent removed under reduced pressure. Purification by flash column chromatography on silica gel (*n*-hexane/EtOAc 7:1 as eluent) gave **3a**.

General procedure for the AuCl/AgOTf-catalyzed tandem amination/ring expansion of 1 with 2: A solution of AuCl (15 μmol) and AgOTf (15 μmol) was stirred in toluene (1.5 mL) under an Ar atmosphere at room temperature for 1 h. Then a toluene solution (1.5 mL) containing **1** (0.3 mmol) and **2** (0.6 mmol) was added to the reaction mixture, which was stirred at 100 °C and monitored to completion by TLC analysis. The reaction mixture was then cooled and the solvent removed under reduced pressure. Purification by flash column chromatography on silica gel (*n*-hexane/EtOAc 7:1 as eluent) gave **3**.

Procedure for the AuCl/AgOTf-catalyzed ring expansion of 6a with 2b: A solution of AuCl (15 μmol) and AgOTf (15 μmol) in toluene (1.5 mL) was stirred at room temperature for 1 h. Then a toluene solution (1.5 mL) containing **6a** (0.3 mmol) and **2b** (0.3 mmol) was added to the reaction mixture, which was stirred at 100 °C for 15 h. The reaction mixture then cooled and the solvent was removed under reduced pressure. Purification by flash column chromatography on silica gel (*n*-hexane/EtOAc = 7:1 as eluent) gave **3a** and **3p**.

Procedure for AuCl/AgOTf-catalyzed ring expansion of 6h: A solution of AuCl (15 μmol) and AgOTf (15 μmol) in toluene (1.5 mL) was stirred under an Ar atmosphere at room temperature for 1 h. Then a toluene solution (1.5 mL) containing **6h** (0.3 mmol) was added to the reaction mixture, which was stirred at 100 °C for 15 h. The reaction mixture was then cooled and the solvent removed under reduced pressure. Purification by flash column chromatography on silica gel (*n*-hexane/EtOAc 7:1 as eluent) gave **3j**.

2-Phenyl-1-tosylpyrrolidine (3a):[19,26,30] White solid; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ = 1.62–1.70 (m, 1H), 1.78–1.90 (m, 2H), 1.94–2.04 (m, 1H), 2.42 (s, 3H), 3.39–3.45 (m, 1H), 3.59–3.64 (m, 1H), 4.79 (dd, 1H, J = 7.6, 3.3 Hz), 7.21–7.30 (m, 7H), 7.67 ppm (d, 2H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ = 21.5, 24.0, 35.8, 49.4, 63.3, 126.2, 127.0, 127.5, 128.3, 129.6, 135.2, 143.1, 143.3 ppm; MS (ESI): m/z: 324 $[M+Na]^+$, 302 $[M+H]^+$.

2-(4-Methylphenyl)-1-tosylpyrrolidine (3b):[19,26,30] White solid; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ = 1.62–1.68 (m, 1H), 1.76–1.98 (m, 3H), 2.32 (s, 3H), 2.42 (s, 3H), 3.37–3.43 (m, 1H), 3.58–3.63 (m, 1H), 4.73 (dd, 1H, J = 7.5, 3.4 Hz), 7.10 (d, 2H, J = 7.9 Hz), 7.20 (d, 2H, J = 8.0 Hz), 7.28 (d, 2H, J = 8.0 Hz), 7.67 ppm (d, 2H, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ = 21.1, 21.5, 24.0, 35.8, 49.4, 63.1, 126.1, 127.5, 129.0, 129.6, 135.2, 136.6, 140.1, 143.2 ppm; MS (ESI): m/z: 338 $[M+Na]^+$, 316 $[M+H]^+$.

2-(4-*tert*-Butylphenyl)-1-tosylpyrrolidine (3c): White solid; m.p. 96–98 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ = 1.30 (s, 9H), 1.63–1.70 (m, 1H), 1.79–1.99 (m, 3H), 2.41 (s, 3H), 3.41–3.47 (m, 1H), 3.58–3.63 (m, 1H), 4.77 (dd, 1H, J = 7.6, 3.4 Hz), 7.19–7.30 (m, 6H), 7.64 ppm (d, 2H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ = 21.5, 24.1, 31.4, 34.4, 35.7, 49.3, 63.0, 125.2, 125.9, 127.5, 129.5, 135.4, 139.8, 143.1, 149.8 ppm; IR (KBr): $\tilde{\nu}$ = 2961, 1341, 1335, 1152, 1105, 1005, 671, 586 cm^{-1}; MS (ESI): m/z: 380 $[M+Na]^+$; HRMS (ESI) calcd for $C_{21}H_{27}NO_2SNa$: 380.1655; found: 380.1786.

2-(4-Methoxyphenyl)-1-tosylpyrrolidine (3d):[26] White solid; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ = 1.63–1.69 (m, 1H), 1.75–1.97 (m, 3H), 2.42 (s, 3H), 3.37–3.44 (m, 1H), 3.57–3.62 (m, 1H), 3.79 (s, 3H), 4.73 (dd, 1H, J = 7.4, 3.6 Hz), 6.83 (d, 2H, J = 8.6 Hz), 7.21–7.28 (m, 4H), 7.66 ppm (d, 2H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ = 21.5, 24.0, 35.8, 49.3, 55.3, 62.8, 113.7, 127.3, 127.5, 129.5, 135.2, 135.2, 143.2, 158.7 ppm; MS (ESI): m/z: 354 $[M+Na]^+$.

2-(3,5-Dimethylphenyl)-1-tosylpyrrolidine (3e): White solid; m.p. 77–79 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ = 1.60–1.67 (m, 1H), 1.76–1.99 (m, 3H), 2.26 (s, 6H), 2.42 (s, 3H), 3.41–3.47 (m, 1H), 3.58–3.63 (m, 1H), 4.72 (dd, 1H, J = 7.2, 3.2 Hz), 6.85 (s, 3H), 7.26 (d, 2H, J = 7.8 Hz), 7.65 ppm (d, 2H, J = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ = 21.4, 21.5, 24.0, 35.9, 49.4, 63.3, 124.0, 127.5, 128.7, 129.5, 135.4, 137.7, 142.9, 143.1 ppm; IR (KBr): $\tilde{\nu}$ = 1605, 1342, 1157, 1094, 1003, 818, 586 cm^{-1}; MS (ESI): m/z: 352 $[M+Na]^+$, 330 $[M+H]^+$; HRMS (ESI) calcd for $C_{19}H_{23}NO_2SNa$: 352.1342; found: 352.1316.

2-(4-Fluorophenyl)-1-tosylpyrrolidine (3f):[31] White solid; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ = 1.62–1.69 (m, 1H), 1.73–1.88 (m, 2H), 1.93–2.04 (m, 1H), 2.42 (s, 3H), 3.37–3.43 (m, 1H), 3.58–3.63 (m, 1H), 4.74 (dd, 1H, J = 7.6, 3.6 Hz), 6.97 (t, 2H, J = 8.7 Hz), 7.26–7.29 (m, 4H), 7.66 ppm (d, 1H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ = 21.5, 23.9, 35.9, 49.4, 62.7, 115.1(d, J=21.4 Hz), 127.5, 127.8 (d, J = 8.0 Hz), 129.6, 134.9, 138.9 (d, J = 2.9 Hz), 143.5, 162.6 ppm (d, J = 243.4 Hz); MS (ESI): m/z: 342 $[M+Na]^+$.

2-(4-Chlorophenyl)-1-tosylpyrrolidine (3g):[26,31] White solid; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ = 1.68–1.87 (m, 3H), 1.95–2.02 (m, 12H), 2.43 (s, 3H), 3.38–3.44 (m, 1H), 3.58–3.63 (m, 1H), 4.72 (dd, 1H, J = 7.8, 3.7 Hz), 7.23–7.30 (m, 6H), 7.66 ppm (d, 1H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ = 21.5, 24.0, 35.8, 49.4, 62.7, 127.5, 127.6, 128.4, 129.7, 132.8, 134.8, 141.7, 143.5 ppm; MS (ESI): m/z: 358 $[M+Na]^+$, 336 $[M+H]^+$.

2-(Naphthalen-1-yl)-1-tosylpyrrolidine (3h):[19] White solid; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ = 1.71–1.90 (m, 3H), 2.06–2.15 (m, 1H), 2.44 (s, 3H), 3.42–3.49 (m, 1H), 3.77–3.82 (m, 1H), 5.57 (d, 1H, J = 6.8 Hz), 7.32 (d, 2H, J = 8.0 Hz), 7.43–7.54 (m, 3H), 7.66 (d, 1H, J = 8.1 Hz), 7.75–7.92 ppm (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ = 21.6, 23.9, 34.6, 49.4, 60.7, 122.8, 123.8, 125.4, 125.9, 127.6, 127.6, 129.0, 129.7, 129.9, 133.9, 134.9, 138.2, 143.4 ppm; MS (ESI): m/z: 374 $[M+Na]^+$, 352 $[M+H]^+$.

2-(2,6-Dimethylphenyl)-1-tosylpyrrolidine (3i): White solid; m.p. 154–155 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ = 1.53–1.61 (m, 1H), 1.89–1.99 (m, 2H), 2.16–2.22 (m, 1H), 2.35 (s, 6H), 2.40 (s, 3H), 3.50–3.57 (m, 1H), 3.82 (t, 1H, J = 9.8 Hz), 5.01 (dd, 1H, J = 9.4, 7.8 Hz), 6.92–7.03 (m, 3H), 7.20 (d, 2H, J = 8.0 Hz), 7.54 ppm (d, 2H, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ = 20.8, 21.5, 25.5, 32.7, 49.3, 60.4, 126.9, 127.4, 129.3, 135.6, 135.9, 136.9, 143.1 ppm; IR (KBr): $\tilde{\nu}$ = 1341, 1157, 1086, 989,

696, 592 cm^{-1}; MS (ESI): *m/z*: 352 $[M+Na]^+$; HRMS (ESI) calcd for $C_{19}H_{23}NO_2SNa$: 352.1342; found: 352.1319.

2-(2-Methoxyphenyl)-1-tosylpyrrolidine (3j):[19,24] White solid; ^1H NMR ($CDCl_3$, 400 MHz, TMS): $\delta = 1.60–1.66$ (m, 1H), 1.70–1.92 (m, 3H), 2.43 (s, 3H), 3.31–3.37 (m, 1H), 3.62–3.67 (m, 1H), 3.80 (s, 3H), 5.10 (dd, 1H, $J = 7.6$, 2.4 Hz), 6.82 (d, 1H, $J = 8.2$ Hz), 6.93 (t, 1H, $J = 7.4$ Hz), 7.19–7.31 (m, 3H), 7.43 (d, 1H, $J = 7.4$ Hz), 7.72 ppm (d, 2H, $J = 8.1$ Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): $\delta = 21.5$, 23.8, 34.0, 49.4, 55.2, 58.8, 110.1, 120.3, 127.3, 127.6, 128.0, 129.5, 131.3, 135.1, 143.1, 155.7 ppm; MS (ESI): *m/z*: 354 $[M+Na]^+$, 332 $[M+H]^+$.

2-Methyl-2-phenyl-1-tosylpyrrolidine (3k):[19] White solid; ^1H NMR ($CDCl_3$, 400 MHz, TMS): $\delta = 1.78–1.89$ (m, 5H), 1.94–2.01 (m, 1H), 2.11–2.17 (m, 1H), 2.41 (s, 3H), 3.52–3.58 (m, 1H), 3.68–3.73 (m, 1H), 7.20–7.31 (m, 5H), 7.39 (d, 2H, $J = 7.4$ Hz), 7.58 ppm (d, 2H, $J = 8.2$ Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): $\delta = 21.5$, 22.5, 26.4, 45.8, 49.8, 69.9, 125.8, 126.6, 127.1, 128.0, 129.3, 138.5, 142.5, 146.5 ppm; MS (ESI): *m/z*: 338 $[M+Na]^+$, 316 $[M+H]^+$.

2-(4-Fluorophenyl)-2-methyl-1-tosylpyrrolidine 3l: White solid; m.p. 109–110 °C; ^1H NMR ($CDCl_3$, 400 MHz, TMS): $\delta = 1.77–1.90$ (m, 5H), 1.94–2.13 (m, 2H), 2.41 (s, 3H), 3.51–3.57 (m, 1H), 3.67–3.72 (m, 1H), 6.93–6.99 (m, 2H), 7.23 (d, 1H, $J = 8.1$ Hz), 7.32–7.38 (m, 2H), 7.58 ppm (d, 2H, $J = 8.2$ Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): $\delta = 21.5$, 22.4, 26.5, 45.8, 49.8, 69.3, 114.7 (d, $J = 21.1$ Hz), 127.1, 127.5 (d, $J = 7.9$ Hz), 129.3, 138.3, 142.5 (d, $J = 40.5$ Hz), 161.6 ppm (d, $J = 243.6$ Hz); IR (KBr): $\tilde{\nu} =$ 2853, 1599, 1508, 1335, 1155, 1005, 814, 665, 550 cm^{-1}; MS (ESI): *m/z*: 356 $[M+Na]^+$; HRMS (ESI) calcd for $C_{18}H_{20}NO_2FSNa$: 356.1091; found: 356.1473.

2-Octyl-1-tosylpyrrolidine (3m): Brown oil; ^1H NMR ($CDCl_3$, 400 MHz, TMS): $\delta = 0.88$ (t, 3H, $J = 6.6$ Hz), 1.18–1.28 (m, 12H), 1.42–1.59 (m, 4H), 1.71–1.84 (m, 2H), 2.42 (s, 3H), 3.15–3.21 (m, 1H), 3.33–3.39 (m, 1H), 3.55–3.60 (m, 1H), 7.29 (d, 2H, $J = 8.0$ Hz), 7.71 ppm (d, 2H, $J =$ 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): $\delta = 14.1$, 21.5, 22.7, 24.1, 26.2, 29.3, 29.6, 30.6, 31.9, 36.5, 48.9, 60.6, 127.5, 129.6, 135.1, 143.1 ppm; IR (KBr): $\tilde{\nu} = 2924$, 1346, 1159, 1094, 8160, 664, 588 cm^{-1}; MS (ESI): *m/z*: 360 $[M+Na]^+$; HRMS (ESI) calcd for $C_{19}H_{31}NO_2SNa$: 360.1968; found: 360.1846.

2-Dodecyl-1-tosylpyrrolidine (3n): Yellow oil; ^1H NMR ($CDCl_3$, 400 MHz, TMS): $\delta = 0.88$ (t, 3H, $J = 6.9$ Hz), 1.27 (s, 20H), 1.53–1.62 (m, 4H), 1.72–1.83 (m, 2H), 2.43 (s, 3H), 3.16–3.22 (m, 1H), 3.34–3.40 (m, 1H), 3.56–3.62 (m, 1H), 7.30 (d, 2H, $J = 7.9$ Hz), 7.71 ppm (d, 2H, $J =$ 8.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): $\delta = 14.1$, 21.5, 22.7, 24.1, 26.2, 29.4, 29.6, 29.6, 29.7, 30.7, 31.9, 36.5, 48.9, 60.6, 127.5, 129.6, 135.1, 143.1 ppm; IR (KBr): $\tilde{\nu} = 2922$, 2853, 1341, 1157, 1091, 806, 667 cm^{-1}; MS (ESI): *m/z*: 416 $[M+Na]^+$; HRMS (ESI) calcd for $C_{23}H_{39}NO_2SNa$: 416.2594; found: 416.3034.

2-Phenethyl-1-tosylpyrrolidine (3o):[32] Yellow oil; ^1H NMR ($CDCl_3$, 400 MHz, TMS): $\delta = 1.43–1.63$ (m, 3H), 1.74–1.83 (m, 2H), 2.18–2.26 (m, 1H), 2.41 (s, 3H), 2.60–2.77 (m, 2H), 3.17–3.23 (m, 1H), 3.38–3.44 (m, 1H), 3.55–3.61 (m, 1H), 7.19–7.32 (m, 7H), 7.62 ppm (d, 2H, $J = 8.1$ Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): $\delta = 21.5$, 24.1, 30.8, 32.4, 37.7, 49.1, 59.8, 125.9, 127.6, 128.4, 128.5, 129.6, 134.7, 141.6, 143.2 ppm; MS (ESI): *m/z*: 352 $[M+Na]^+$, 330 $[M+H]^+$.

2-Phenyl-1-(phenylsulfonyl)pyrrolidine (3p):[19] White solid; ^1H NMR ($CDCl_3$, 400 MHz, TMS): $\delta = 1.63–2.05$ (m, 4H), 3.43–3.49 (m, 1H), 3.61–3.66 (m, 1H), 4.82 (dd, 1H, $J = 7.7$, 3.5 Hz), 7.20–7.30 (m, 5H), 7.46–7.58 (m, 3H), 7.77–7.79 ppm (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): $\delta =$ 24.0, 35.8, 49.4, 63.4, 126.2, 127.1, 127.4, 128.3, 129.0, 132.6, 138.1, 142.9 ppm; MS (ESI): *m/z*: 310 $[M+Na]^+$.

1-(4-Bromophenylsulfonyl)-2-phenylpyrrolidine (3q): Pale yellow oil; ^1H NMR ($CDCl_3$, 400 MHz, TMS): $\delta = 1.70–2.10$ (m, 4H), 3.43–3.49 (m, 1H), 3.59–3.64 (m, 1H), 4.79 (dd, 1H, $J = 7.7$, 3.6 Hz), 7.23–7.30 (m, 5H), 7.58 ppm (s, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): $\delta = 24.1$, 35.9, 49.4, 63.5, 126.2, 127.2, 127.4, 128.4, 128.9, 132.2, 137.5, 142.5 ppm; IR (KBr): $\tilde{\nu} = 2973$, 1347, 1342, 1155, 1114, 692 cm^{-1}; MS (ESI): *m/z*: 388 $[M+Na]^+$; HRMS (ESI) calcd for $C_{16}H_{16}NO_2BrSNa$: 387.9983; found: 387.9975.

1-(4-Nitrophenylsulfonyl)-2-phenylpyrrolidine (3r):[19,26] White solid; ^1H NMR ($CDCl_3$, 400 MHz, TMS): $\delta = 1.80–2.22$ (m, 4H), 3.43–3.49 (m, 1H), 3.58–3.67 (m, 1H), 4.87 (dd, 1H, $J = 7.8$, 4.3 Hz), 7.16–7.26 (m, 5H), 7.79–7.81 (m, 2H), 8.22–8.24 ppm (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): $\delta = 24.3$, 36.0, 49.5, 63.7, 124.0, 126.4, 127.5, 128.3, 128.4, 141.8, 144.7, 149.8 ppm; MS (ESI): *m/z*: 355 $[M+Na]^+$.

(*E*)-4-Methyl-*N*-(4-phenylbut-3-enyl)benzenesulfonamide (4a):[19,30] Colourless oil; ^1H NMR ($CDCl_3$, 400 MHz, TMS): $\delta = 2.36$ (q, 2H, $J =$ 6.8 Hz), 2.41 (s, 3H), 3.09 (q, 2H, $J = 6.5$ Hz), 4.63 (t, 1H, $J = 5.8$ Hz), 5.94–6.01 (m, 1H), 6.35 (d, 1H, $J = 15.8$ Hz), 7.20–7.31 (m, 7H), 7.75 ppm (d, 2H, $J = 8.2$ Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): $\delta = 21.5$, 33.0, 42.6, 125.6, 126.1, 127.2, 127.5, 128.6, 129.7, 133.2, 136.8, 137.0, 143.5 ppm; MS (ESI): *m/z*: 324 $[M+Na]^+$.

***N*-(4,4-Diphenylbut-3-enyl)-4-methylbenzenesulfonamide (4b)**:[33,34] Yellow oil; ^1H NMR ($CDCl_3$, 400 MHz, TMS): $\delta = 2.26$ (q, 2H, $J =$ 7.1 Hz), 2.40 (s, 3H), 3.03 (q, 2H, $J = 6.6$ Hz), 4.59 (t, 3H, $J = 6.0$ Hz), 5.90 (t, 1H, $J = 7.4$ Hz), 7.08–7.36 (m, 12H), 7.69 ppm (d, 2H, $J = 8.2$ Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): $\delta = 21.6$, 29.9, 43.1, 124.6, 127.1, 127.3, 127.3, 127.3, 128.2, 128.4, 129.7, 129.7, 136.9, 139.5, 142.0, 143.4, 144.7 ppm; MS (ESI): *m/z*: 400 $[M+Na]^+$, 378 $[M+H]^+$.

4-Methyl-*N*-(6-*p*-tolylhex-3-en-5-ynyl)benzenesulfonamide (4c): Yellow oil; ^1H NMR ($CDCl_3$, 400 MHz, TMS): $\delta = 2.28–2.42$ (m, 14H), 2.25–2.27 (q, 2H, $J = 6.4$ Hz), 3.03–3.13 (m, 4H), 5.54–5.58 (m, 2H), 5.66–5.83 (m, 3Hz), 5.94–6.01 (m, 1H), 7.10–7.14 (m, 4H), 7.24–7.32 (m, 8H), 7.73–7.76 ppm (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): $\delta = 21.5$, 21.5, 30.3, 33.2, 42.2, 42.2, 84.8, 86.7, 89.5, 95.0, 112.6, 113.3, 120.0, 120.0, 127.1, 129.1, 129.1, 129.7, 129.8, 131.4, 131.4, 136.9, 138.0, 138.4, 138.6, 138.9, 143.4, 143.6 ppm; IR (KBr): $\tilde{\nu} = 3291$, 2920, 2265, 1327, 1159, 1094, 816, 664 cm^{-1}; MS (ESI): *m/z*: 362 $[M+Na]^+$; HRMS (ESI) calcd for $C_{20}H_{21}NO_2SNa$: 362.1185; found: 362.1031.

4-Methyl-*N*,*N*-bis[(*E*)-4-phenylbut-3-enyl]benzenesulfonamide (5a):[19] Colorless oil; ^1H NMR ($CDCl_3$, 400 MHz, TMS): $\delta = 2.39$ (s, 3H), 2.49 (q, 4H, $J = 7.2$ Hz), 3.30 (t, 4H, $J = 7.2$ Hz), 6.05–6.12 (m, 2H), 6.39 (d, 2H, $J = 15.8$ Hz), 7.19–7.29 (m, 12H), 7.71 ppm (d, 2H, $J = 8.3$ Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): $\delta = 21.5$, 32.7, 48.1, 126.1, 126.2, 127.2, 127.3, 128.5, 129.7, 132.3, 137.2, 143.2 ppm; MS (ESI): *m/z*: 454 $[M+Na]^+$.

General procedure for AuCl/AgOTf-catalyzed amination of 1a, 1d, 1f, and 1h–j with 2a: A solution of AuCl (15 μmol) and AgOTf (15 μmol) in toluene (1.5 mL) was stirred at room temperature for 1 h. Then a toluene solution (1.5 mL) containing **1** (0.3 mmol) and **2a** (0.6 mmol) was added to the reaction mixture, which was stirred at room temperature and monitored to completion by TLC analysis. The reaction mixture was then cooled and the solvent removed under reduced pressure. Purification by flash column chromatography on silica gel (*n*-hexane/EtOAc 7:1 as eluent) gave **6**.

***N*-[Cyclopropyl(phenyl)methyl]-4-methylbenzenesulfonamide (6a)**: White solid; m.p. 127–128 °C; ^1H NMR ($CDCl_3$, 400 MHz, TMS): $\delta =$ 0.20–0.30 (m, 2H), 0.43–0.53 (m, 2H), 1.05–1.14 (m, 1H), 2.37 (s, 3H), 3.70 (dd, 1H, $J = 8.4$, 6.0 Hz), 5.16 (d, 1H, $J = 5.6$ Hz), 7.13–7.18 (m, 7H), 7.56 ppm (d, 2H, $J = 8.1$ Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): $\delta = 3.8$, 4.5, 18.1, 21.5, 62.5, 126.9, 127.1, 127.4, 128.3, 129.3, 137.8, 140.4, 143.0 ppm; IR (KBr): $\tilde{\nu} = 3250$, 2927, 14521, 1346, 1160, 1088, 1043, 822, 679 cm^{-1}; MS (ESI): *m/z*: 324 $[M+Na]^+$; HRMS (ESI) calcd for $C_{17}H_{19}NO_2SNa$: 324.1029; found: 324.0650.

***tert*-Butylcyclopropyl(phenyl)methylcarbamate (6b)**: White solid; m.p. 71–72 °C; ^1H NMR ($CDCl_3$, 400 MHz, TMS): $\delta = 0.33–0.60$ (m, 4H), 1.05–1.13 (m, 1H), 1.41 (s, 9H), 4.12 (brs, 1H), 5.00 (brs, 1H), 7.22–7.33 ppm (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): $\delta = 3.6$, 17.3, 28.4, 58.4, 79.4, 126.5, 127.1, 128.1, 128.4, 142.7, 155.4 ppm; IR (KBr): $\tilde{\nu} = 3383$, 1680, 1522, 1177, 1017, 878, 754, 702 cm^{-1}; MS (ESI): *m/z*: 270 $[M+Na]^+$; HRMS (ESI) calcd for $C_{15}H_{21}NO_2Na$: 270.1465; found: 270.1363.

Benzylcyclopropyl(phenyl)methylcarbamate (6c): White solid; m.p. 60–61 °C; ^1H NMR ($CDCl_3$, 400 MHz, TMS): $\delta = 0.33–0.61$ (m, 4H), 1.11–1.13 (m, 1H), 4.16 (brs, 1H), 4.99–5.11 (m, 2H), 5.26 (brs, 1H), 7.23–7.33 ppm (m, 10H); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): $\delta = 3.7$, 3.8, 17.2, 59.2, 66.8, 126.5, 127.3, 128.1, 128.5, 136.5, 142.2, 155.9 ppm; IR (KBr): $\tilde{\nu} = 3337$, 1682, 1528, 1265, 1040, 878, 756, 698 cm^{-1}; MS (ESI): *m/z*: 304

$[M+Na]^+$; HRMS (ESI) calcd for $C_{18}H_{19}NO_2Na$: 304.1308; found: 304.1348.

***N*-[Cyclopropyl(4-methoxyphenyl)methyl]-4-methylbenzenesulfonamide (6d)**: White solid; m.p. 124–125 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ = 0.17–0.26 (m, 2H), 0.38–0.51 (m, 2H), 1.04–1.12 (m, 1H), 2.37 (s, 3H), 3.66 (dd, 1H, J = 8.3, 6.0 Hz), 3.75 (s, 3H), 5.28 (d, 1H, J = 6.6 Hz), 6.69 (d, 2H, J = 8.7 Hz), 7.03 (d, 2H, J = 10.0 Hz), 7.14 (d, 1H, J = 8.0 Hz), 7.56 ppm (d, 1H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ = 3.6, 4.4, 18.0, 21.5, 55.2, 61.9, 113.6, 127.2, 128.0, 129.2, 132.7, 137.9, 142.9, 158.8 ppm; IR (KBr): $\tilde{\nu}$ = 3237, 1612, 1514, 1437, 1323, 1242, 1155, 1049, 806, 669 cm^{-1}; MS (ESI): m/z: 354 $[M+Na]^+$; HRMS (ESI) calcd for $C_{18}H_{21}NO_3SNa$: 354.1134; found: 354.1085.

***N*-[Cyclopropyl(4-fluorophenyl)methyl]-4-methylbenzenesulfonamide (6e)**: White solid; m.p. 100–102 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ = 0.16–0.27 (m, 2H), 0.43–0.52 (m, 2H), 1.03–1.09 (m, 1H), 2.38 (s, 3H), 3.66 (dd, 1H, J = 8.4, 6.0 Hz), 5.41 (d, 1H, J = 5.7 Hz), 6.82–6.86 (m, 2H), 7.07–7.16 (m, 4H), 7.55 ppm (d, 2H, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ = 3.7, 4.4, 18.1, 21.5, 61.9, 115.0 (d, J = 21.2 Hz), 127.1, 128.5 (d, J = 8.0 Hz), 129.3, 136.4 (d, J = 3.2 Hz), 137.7, 143.2, 162.8 ppm (d, J = 244.3 Hz); IR (KBr): $\tilde{\nu}$ = 3237, 1612, 1514, 1437, 1323, 1242, 1155, 1049, 806, 669, 544 cm^{-1}; MS (ESI): m/z: 342 $[M+Na]^+$; HRMS (ESI) calcd for $C_{17}H_{18}NO_2FSNa$: 342.0934; found: 342.1003.

***N*-[Cyclopropyl(naphthalen-1-yl)methyl]-4-methylbenzenesulfonamide (6f)**: White solid; m.p. 119–120 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ = 0.20- 0.32 (m, 2H), 0.37–0.53 (m, 2H), 1.34–1.43 (m, 1H), 2.24 (s, 3H), 4.61 (t, 1H, J = 7.2 Hz), 5.51 (d, 1H, J = 6.0 Hz), 6.89 (d, 2H, J = 8.2 Hz), 7.24–7.45 (m, 6H), 7.65 (d, 1H, J = 8.1 Hz), 7.44–7.77 (m, 1H), 8.01–8.02 ppm (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ = 3.5, 5.3, 17.4, 21.3, 58.8, 123.2, 125.1, 125.3, 125.5, 126.1, 127.0, 128.1, 128.7, 128.9, 130.7, 133.7, 135.5, 137.5, 142.7 ppm; IR (KBr): $\tilde{\nu}$ = 3254, 1597, 1508, 1443, 1163, 773, 671, 570 cm^{-1}; MS (ESI): m/z: 374 $[M+Na]^+$; HRMS (ESI) calcd for $C_{21}H_{21}NO_2SNa$: 374.1191; found: 374.1369.

***N*-[Cyclopropyl(3,5-dimethylphenyl)methyl]-4-methylbenzenesulfonamide (6g)**: White solid; m.p. 104–105 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ = 0.24–0.31 (m, 2H), 0.41–0.53 (m, 2H), 1.04–1.13 (m, 1H), 2.16 (s, 6H), 2.37 (s, 3H), 3.62 (dd, 1H, J = 8.4, 6.1 Hz), 5.15 (d, 1H, J = 5.9 Hz), 6.64 (s, 2H), 6.77 (s, 1H), 7.13 (d, 2H, J = 8.1 Hz), 7.54 ppm (d, 2H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ = 3.7, 4.5, 18.0, 21.2, 21.4, 62.6, 124.7, 127.2, 129.0, 129.1, 137.7, 137.9, 140.2, 142.8 ppm; IR (KBr): $\tilde{\nu}$ = 3262, 3009, 2918, 1431, 1333, 1163, 1096, 1026, 812, 712, 662 cm^{-1}; MS (ESI): m/z: 352 $[M+Na]^+$; HRMS (ESI) calcd for $C_{19}H_{23}NO_2SNa$: 352.1342; found: 352.1355.

***N*-[Cyclopropyl(2-methoxyphenyl)methyl]-4-methylbenzenesulfonamide (6h)**:[24] White solid; m.p. 136–138 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ = 0.19–0.24 (m, 1H), 0.33–0.40 (m, 2H), 0.47–0.53 (m, 1H), 1.28–1.36 (m, 1H), 2.28 (s, 3H), 3.66–3.70 (m, 4H), 5.84 (d, 1H, J = 9.1 Hz), 6.60 (d, 1H, J = 8.2 Hz), 6.71 (t, 1H, J = 7.4 Hz), 6.84–7.10 (m, 4H), 7.45 ppm (d, 2H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ = 4.2, 4.9, 16.8, 21.4, 55.1, 61.7, 110.6, 120.4, 126.8, 128.0, 128.4, 128.8, 129.0, 137.9, 142.4, 156.2 ppm; IR (KBr): $\tilde{\nu}$ = 3281, 2928, 1601, 1497, 1423, 1325, 1159, 762, 679 cm^{-1}; MS (ESI): m/z: 354 $[M+Na]^+$; HRMS (ESI) calcd for $C_{18}H_{21}NO_3SNa$: 354.1134; found: 354.1089.

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