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Gold- and Silver-Catalysed Cyclisation Reactions of β-Amino Allenes

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Abstract

Herein we report the formation of pyrrolines and tetrahydropyridines from the cyclisation reactions of β-amino allenes by both Au^I and Ag^I catalysts in yields ranging from 5 to 70 %. Au^I catalysts favour a 5-*endo-dig* cyclisation before rapid rearrangement to the 5-*exo-dig* product, while AgI favours a 6-*endo-trig* cyclisation. We also report the first known Ag_2O catalysed cyclisation reaction of an allene which occurred in good yield (61 %).

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Gold- and Silver-Catalysed Cyclisation Reactions of β-Amino Allenes

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Here we report the formation of pyrrolines and tetrahydropyridines from the cyclisation reactions of β-amino allenes by both Au(I) and Ag(I) catalysts in yields ranging from 5 – 70%. Au(I)-catalysts favour a 5-*endo-dig* cyclisation before rapid rearrangement to the 5-*exo-dig* product, while Ag(I) favours a 6-*endo-trig* cyclisation. We also report the first known Ag_2O catalyzed cyclisation reaction of an allene which occurred in good yield (61%).

Introduction

The synthesis of functionalized azetidines, pyrrolines and tetrahydropyridines is an important field of synthetic chemistry research because of their presence in the skeleton of many alkaloids and pharmaceutically relevant products (Figure 1). The alkaloids (+)-cannabisativine,[1] plakoridine A,[2] and panaresidin A[3] contain a tetrahydropyridine, pyrroline and azetidine ring, respectively. The pharmaceuticals imipenem (antibacterial), [4] and tiagabine (neutoprotector)[5] contain a pyrroline and tetrahydropyridine ring.

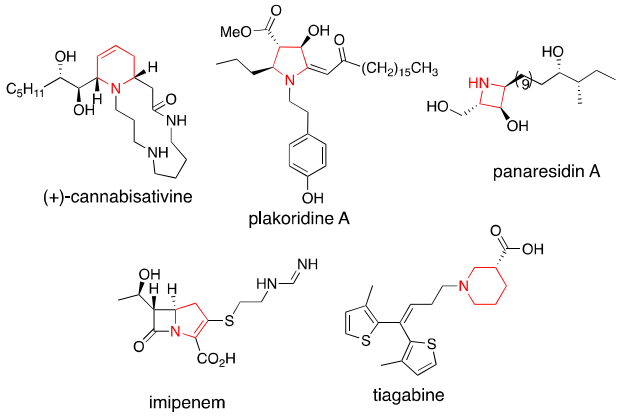


Figure 1: Representative examples of alkaloids and drugs bearing azetidine, pyrroline and tetrahydropyridine core units.

Gold- and silver-catalysed cyclisation reactions of allenes bearing pendant heteroatoms is an expedient and atom efficient method to form nitrogen-containing heterocycles.[6] For example, $AuCl_3$ has successfully catalyzed the formation of 3-pyrrolines from α-aminoallenes.[7] Meanwhile $AgNO_3$ has been used to synthesise chiral Δ^3-pyrrolines by the cyclisation of α-aminoallenes (Figure 2. **a**).[8] Due to the complete retention of stereochemical information in chiral allenic substrates, several total synthesis routes have included gold- and silver-catalyzed cyclisations in the formation of enantiomerically enriched biologically active alkaloids including (−)-sedinine,[9] swainsonine,[10] (+)-sedamine,[11] and the nuphar alkaloids.[12]

While there has been strong focus on investigating the cyclisation of α-aminoallenes in the presence of cationic transition metals, the reactivity of homologous β-amino allenes has focused mainly on Pd(0)-allylic activation/redox coupling reactions.[13] The Au(I)- or Ag(I)-catalysed cyclisations of the β-amino allenes has been far less investigated.

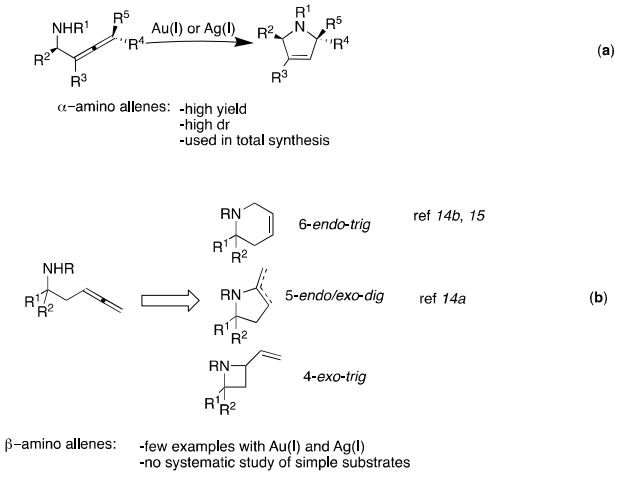


Figure 2: Comparative reports of amino allenes (a) Au(I)- and Ag(I)-catalysed cyclisation of α-aminoallenes (b) Possible cyclisation products of β-amino allenes using Au(I) and Ag(I).

Recently β-amino-γ-hydroxyallenes have been shown to undergo a Au(I)-catalysed cyclisation and subsequent elimination to form hydroxymethylpyrroles that were sensitive towards decomposition.[14a] Interestingly, *syn*-β-amino allene-tethered indolizidines have been shown to lead to 6-*endo* adducts while their *anti*-counterparts give an initial 5-*exo* reaction product, however, this represents a special subclass of

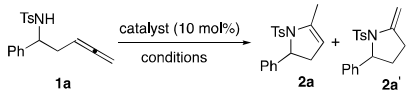
β-amino allene.[15] More recently, Au(I) redox catalysis has been deployed for the 6-*endo*-cyclisation of trisubstituted β-amino allenes with concomitant coupling of diazonium salts to yield aryl-substituted tetrahydropyridines.[14b] The only report of a Ag(I)-catalysed β-amino allene is a single example noted in a footnote of a paper reporting a high yield of 1-tosyl-1,2,3,6-tetrahydropyridine formed by 6-*endo*-cyclisation (Figure 2. b)[13c]

Consequently, the β-amino allenes remain a drastically understudied system in Ag(I)- and Au(I)- catalysis. Their cyclisation reactions would offer a useful route to heterocycle formation as they have the potential to form piperidines, pyrrolines or azetidines (Figure 2. b). Herein, we report the cyclisation of β-amino allenes in the presence of both Au- and Ag-catalysts and compare the regioselectivity of these processes. As far as the authors are aware, this is the first study directly comparing Au(I) and Ag(I) as catalysts in allenic cyclisation reactions.

Results and Discussion

Following the synthesis of β-amino allenes **1a-g**[16] we began investigating their cyclisation reactions in the presence of gold-catalysts using **1a** and the results are summarized in Table 1. β-amino allene **1a** gave white crystals suitable for X-ray structure analysis (Figure 3). Initial results using $(PPh_3)AuCl/AgBF_4$ in dichloromethane at room temperature gave an inseparable mixture of pyrrolidines **2a** and **2a'** in 55% yield in which the endocyclic alkene isomer (**2a**) was favoured (1:1.7). The product mixture, however, was highly crystalline and **2a** was obtained as a single crystal and its structure unambiguously confirmed by X-ray structure analysis (Figure 3).

Table 1: Gold-Catalysed cyclisations of 1a



Entry	Catalyst	Conditions	[a] % (yield)
1	$(PPh_3)AuCl/AgBF_4$	CH_2Cl_2, rt, 46 h	55% **2a/2a'** (1:1.7)
2	AuCl	CH_2Cl_2, reflux, 5 d	19% **2a**
[c]3	[b]$(PMe_3)AuCl/AgBF_4$	DCE, reflux, 24 h	10% **2a**
[d]4	(IPr)AuCl/$AgBF_4$	DCE, rt, 24 h	47% (1:3.2) **2a/2a'**
[e]5	(IPr)AuCl/$AgBF_4$	DCE, reflux, 8 h	57% (1:1.05) [h] **2a/2a'**
6	$(PPh_3)AuCl/AgBF_4$	Toluene, rt, 3 d	NR
[f]7	$(PPh_3)AuCl/AgBF_4$	CH_3CN, rt, 30 min	70% (1.5:1) **2a/2a'**
[g]8	$(PPh_3)AuCl/AgBF_4$	THF, rt, 38 h	65% **2a/2a'** (1:1)

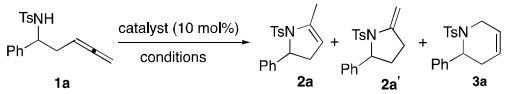
[a] Isolated yield. [b] 20 mol% catalyst. % conversion to methyl ketone determined from ^{1}H NMR of crude reaction materials; [c] 22 %, [d] 26%, [e] 28%, [f] 18%, [g] 35%. [h] Trace quantities of **3a** detected.

Using AuCl as catalyst gave a poor yield of **2a**, while $(Me_3P)AuCl/AgBF_4$ gave a lower yield of the dihydropyrrole **2a** - most likely due to lower Lewis acid character of the Au(I) catalyst (Entry 2 and 3). The *N*-heterocyclic carbene Au(I) complex (IPr)AuCl (IPr = 1,3-bis(2,6-diisopropylphenyl-imidazol-2-ylidene) performed effectively in 1,2-dichloroethane solvent giving 47% yield in a ratio of 1:3.2 (Entry 4). The yield increased when raising the temperature but the selectivity of the rings formed was lowered with trace amounts of 6-membered **3a** formed (Entry 5). Further, in entries 3-5 and 7-8, a methyl ketone side product was able to be isolated, from the hydrolysis of the allene by adventitious water.[17]

Next the effect of solvent with the optimum $(PPh_3)AuCl/AgBF_4$ catalyst system was investigated. In toluene solvent (entry 6) no reaction occurred and only starting material was recovered and the best result was in acetonitrile with a 70% isolated yield favoring **2a** (**2a/2a' =** 1.5:1) in 30 min (entry 7). In tetrahydrofuran solvent the Au(I)-catalyst gave good a yield of 65% of **2a** and **2a'** in a 1:1 ratio (entry 8). Due to the highest isolated yield of **2a** and **2a'** occurring in acetonitrile solvent these conditions were chosen as the optimum Au(I)-catalysed cyclisation reaction for further substrate scope.

Silver catalysts were then screened against the same β-amino allene **1a** and the results are summarized in Table 2.

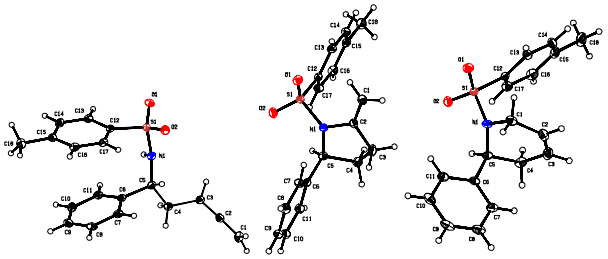
Table 2: Silver-Catalysed Cyclisation of 1a



Entry	Catalyst	Conditions	[a] % (yield)
[d]1	$AgNO_3$	Acetone, rt, 32 h (then 60 °C, 43 h)	5% **3a**
[e]2	$AgBF_4$	CH_2Cl_2, rt, 30 h	56% **3a**
3	Ag_2O	Acetone, rt, 28 h	61% **2a/2a'** (1:2.8)
4	[b]KO^tBu	THF, 40 °C, 3 d, reflux, 56 h	58% **2a/2a'** (4:1)
5	$AgBF_4$	Toluene 22h	68% **2a/2a'** (1:9.1)
6	$AgBF_4$	CH_3CN, 15 h	[c]
7	$AgBF_4$	THF, 30 min	[c]

8	$AgBF_4$	Et_2O, 21 h		44% **3a**

[a] Isolated yields. [b] 1.2 equiv KO^{t}Bu. [c] Recovered starting material. % conversion to methyl ketone determined from ^{1}H NMR of crude reaction material; [d] 13%, [e] 40%.



1a **2a'** **3a**

Figure 3: ORTREP representations of structures **1a**, **2a'** and **3a**.[18]

Curiously, the cyclisation reaction of **1a** using $AgNO_3$ successfully formed the tetrahydropyridine **3a** in low yield rather than the pyrrolidines observed for the gold-catalysts (Entry 1). $AgBF_4$ gave **3a** in a higher 56 % yield at room temperature after 30 h (Entry 2) as white crystals in sufficient quality for structure confirmation by X-ray analysis (Figure 3). Interestingly, Ag_2O used in catalytic quantities (Entry 3) gave a combined yield of 61 % of **2a** and **2a'** in a ratio of 1 : 2.8. As far as the authors are aware, this is the first example of Ag_2O being used as a catalyst for the cyclisation of allenic substrates. To understand whether the Ag_2O catalyst could activate the allene as a Lewis acid or if cyclisation is occurring from Ag_2O acting as a base or both; [19] KO^{t}Bu in stoichiometric quantities was used instead of Ag_2O (Entry 4). This reaction successfully formed a mixture of **2a** and **2a'** in 58 % yield but with the product ratio reversed (**2a**:**2a'** 4:1) and the reaction rate much slower. This suggests that the Ag_2O was most likely acting as both a base and an electrophile.

To understand the effect of solvent on the Ag(I)-catalysed reactions we chose $AgBF_4$ as catalyst. When moving from dichloromethane to toluene, the products formed were the 5-*endo*/*exo*-*dig* products with the *endo* product **2a'** in clear excess of 1:9.1 (Entry 5). This represents a curious switch in regioselectivity compared to the use of dichloromethane as the solvent. However, in acetonitrile or tetrahydrofuran, no reaction was observed and only recovered starting material was obtained (Entries 6 and 7). The use of diethylether gave 44% isolated yield this time of the tetrahydropyridine **3a**.

Due to different ratios of **2a** and **2a'** obtained under different reaction conditions a ^{1}H NMR experiment of the reaction of **1a** with $(PPh_3)AuCl/AgBF_4$ in $CDCl_3$ was performed (Figure 4). Comparing the integration signals of **2a** (the singlet at 4.89 ppm corresponding to its olefinic-*H*) and **2a'** (the singlet at 4.43 ppm corresponding to one of the exocyclic protons) indicated that the β-amino allene was undergoing an initial 5-*endo-dig* cyclisation to **2a'**, then isomerising to **2a** *in situ* – the latter being the more thermodynamically stable product. After a period of 3 days almost all of **2a'** had rearranged to **2a**.[20]

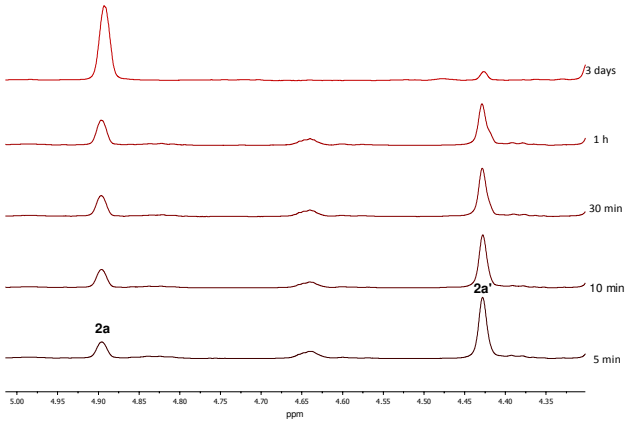


Figure 4: ^{1}H NMR-monitoring ($CDCl_3$) of the cyclisation reaction of **1a** with Au(I).

With these results in hand the remaining synthesised allenes were tested against the best results for both silver- and gold- catalysts, highlighted in Tables 1 and 2 . These results are summarized in Table 3.

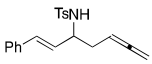
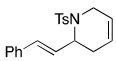
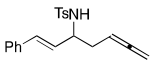
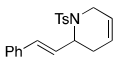
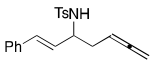
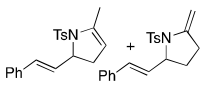
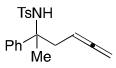
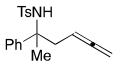
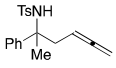
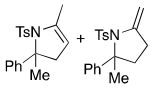
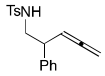
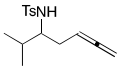
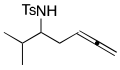
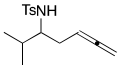
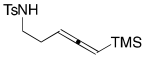
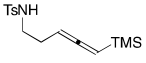
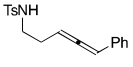
The allene **1b**, substituted with the conjugated cinnamyl group, successfully underwent cyclisation with Ag(I)-catalysts to give the tetrahydropyridine **3b** in moderate yields (45 and 53%, entry 1 and 2). Curiously, the regiochemical switch observed for **1a** when changing between dichloromethane and toluene solvents was not observed for **1b** or any other allenes in Table 3. Treating the same allene with gold catalyst (entry 3) gave a mixture of the *endo*/*exo* alkene products **2b** and **2b'** in low yield (24 %) but with clear preference of **2b** over **2b'** (14.8 : 1 *endo*:*exo*).

The β,β-disubstituted allene **1c**, also underwent successfully cyclisation using both Ag(I)-catalysts to give the 6-*endo-trig* product **3c** in moderate yields (entries 4-5). Notably in toluene the reaction required heat and longer reaction time (entry 5). In contrast, using the optimal gold catalyst conditions, the pyrrolidines **2c** and **2c'** were formed in low yield (12%) but with clear selectivity of **2c** over **2c'** (4.3:1). The α-phenyl substituted allene **1d** cyclised in a 6-*endo-trig* fashion to give **3d** (15% yield) with $AgBF_4$ (entry 7) but only with the addition of heat, suggesting that steric bulk around the allene moeity has significant impact on its capacity to undergo cyclisation.[21]

When β-*iso*propyl allene, **1e**, was used the cyclisation reactions failed to give the desired products (entry 8-10). However, either no reaction was observed or hydrolysis of the allene to the corresponding methyl ketone was observed

We then investigated two allenes substituted at the terminal position, **1f** and **1g**. Allene **1g** cyclised to **2g'** during its synthesis without the addition of any Au(I)- or Ag(I)-catalyst, likely due to the electron withdrawing capacity of the phenyl group in conjugation with the distal bond of the allene.[16] In contrast the terminal TMS allene **1f** failed to yield any successful cyclised product (entry 11-13). This may be due to the steric bulk of the TMS group preventing the gold or silver catalyst from activating the allene bonds towards nucleophilic attack.

Table 3: Substrate scope of β-amino allene cyclisations

Entry		Allene	Catalyst	Conditions		Product	[a]% Yield
1	**1b**		$AgBF_4$	CH_2Cl_2, 40 h, rt	**3b**		45[b]
2	**1b**		$AgBF_4$	Toluene, 58 h, rt	**3b**		53[c]
3	**1b**		$(PPh_3)AuCl$/ $AgBF_4$	CH_3CN, 1 h, rt	**2b + 2b'**		24 (14.8:1)[d]
4	**1c**		$AgBF_4$	CH_2Cl_2, 46 h, rt	**3c**		25
5	**1c**		$AgBF_4$	Toluene, 90 h, 60 ℃	**3c**		42
6	**1c**		$(PPh_3)AuCl$/ $AgBF_4$	CH_3CN, 2.5 h, rt	**2c + 2c'**		12 (4.3:1)
7	**1d**		$AgBF_4$	DCE, reflux, 20 h	**3d**		15
8	**1e**		$AgBF_4$	CH_2Cl_2	-		hydrolysis[e]
9	**1e**		$AgBF_4$	Toluene	-		NR
10	**1e**		$(PPh_3)AuCl$/ $AgBF_4$	CH_3CN	-		hydrolysis[f]
11	**1f**		$AgBF_4$	DCE, reflux, 48 h			NR
12	**1f**		$(PPh_3)AuCl$/ $AgBF_4$	CH_3CN, reflux, 5 h			hydrolysis[g]
13	**1g**		-		**2g'**		2[h]

[a] Isolated Yield. % yield as ketone; [b] 38%, [c] 34%, [d] 69%, [e] 95%, [f] 56%. [g] Could see evidence in the ^1H NMR of the crude reaction material of formation of corresponding ketone but was unable to be isolated. [h] Yield calculated from alcohol starting material.

It was of interest that the switch in regioselectivity of **1a** from using $AgBF_4$ in CH_2Cl_2 solvent (Table 2, entry 2) and $AgBF_4$ in toluene (Table 2, entry 5) was not further demonstrated by the allenes in Table 3. The reason for this switch in regioselectivity is not yet understood. However, the proximity of an unhindered aromatic ring at the β-position being necessary for the switch may indicate some form of π-Ag interaction being involved.

The reasons behind the fascinating switch in regioselectivity between the optimised gold-catalysed cyclisation reactions and optimised silver-catalysed reactions are still being investigated. However, it appears that in β-amino allenes preferential binding of gold catalysts to the proximal double bond of the allene occurs, while silver binds at the distal double bond. It is plausible that the steric bulk of the triphenylphosphine ligands may be responsible for this divergence in comparison to the smaller silver-catalysts, as well as the kinetic favourability in forming 5 membered rings over 6.

Conclusions

In summary, we have successfully shown that β-amino allenes can be cyclised by both Ag(I) and Au(I) catalysts in low to good yields with a divergence in selectivity between the size of the heterocyclic ring formed depending on both catalyst and solvent choice. This is particularly important, as previously only disubstitued β-amino allenes were able to undergo 6-endo-cyclisation with the unsubstituted systems forming 5-membered rings[14b] – here we demonstrate that Ag-catalysts can overcome this limitation. We have also shown the first published example of Ag_2O being used as an allene cyclisation catalyst.

Experimental

See supporting information for synthesis of allene starting materials as well as the synthesis of **2g'.**

General Procedure for Silver Catalysed Cyclisation reactions of allenes:

To an oven dried round bottom flask was added allene **1a** (0.096 mmol, 30 mg, 1 equiv) and the system was purged with N_2 three times in the dark. In a separate oven dried round bottom flask was added $AgBF_4$ (0.0097 mmol, 1.9 mg, 0.1 equiv) before being dissolved in CH_2Cl_2 (1 mL) in the dark. This solution was then added to the flask containing the allene via syringe at room temperature. The reaction mixture was stirred until TLC analysis indicated consumption of starting material before passing through a short plug of silica gel with washing with EtOAc. The title compound **3a** was then purified by silica gel column chromatography (90:8:2 *n*-hex:EtOAc:Et_3N). Any methyl ketone products had lower R_f values than the heterocyclic products and were isolated from the same columns.

2-Phenyl-1-(4-methyl-N-*benzenesulfonamide)-1,2,3,6-tetrahydropyridine* (**3a**)

Following the general method starting with **1a**, (0.096 mmol, 30 mg) **3a** was obtained following silica gel column chromatography (90:8:2 *n*-hex:EtOAc:Et_3N) as a white crystal (16.7 mg, 56%). The spectroscopic matched with those previously reported.[22]

R_f (80:20 PE:EtOAc) = 0.52. mp 116 °C**.** IR(neat): ν_{max}/cm^{-1} 2926 w, 1339 s, 1158 s, 1089 m, 744 m, 700 m, 665 m, 649 m. δ_H (500 MHz, $CDCl_3$) 7.69 (d, *J* 8, 2H, Ar*H*), 7.36-7.23 (m, 7H, Ar*H*), 5.78 (s, 1H, NCH_2CH=CH), 5.60 (d, *J* 10.5, 1H, NCH_2CH=C*H*), 5.30 (d, *J* 5.5, 1H, NC*H*), 4.10 (d, *J* 18.5, 1H, NC*H*H), 3.39 (d, *J* 18.5, 1H, NHCH*H*), 2.41 (s and m, 5H, CH_3 and CHCH_2). δ_C (125 MHz, $CDCl_3$) 143.2 (Ar*C*), 139.4 (Ar*C*), 138.0 (Ar*C*), 129.7 (Ar*C*), 128.5 (Ar*C*), 127.6 (Ar*C*), 127.5 (Ar*C*), 127.2 (Ar*C*), 124.1 (NCH_2CH=*C*H), 123.9 (NCH_2CH=CH), 53.0 (N*C*H), 41.0 (N*C*H_2), 26.6 (NCH*C*H_2), 21.6 (*C*H_3). (HRESI-MS) 336.1027 $C_{18}H_{19}NSO_2Na$ [M + Na]$^+$; 336.1024, required.

(E)-*2-Styryl-1-(4-methyl*-N-*benzenesulfonamide)-1,2,3,6-tetrahydropyridine* **(3b)**

Table 3, entry 1: Following the general procedure allene **1b** (0.15 mmol, 50 mg) was treated with $AgBF_4$ (0.015 mmol, 2.9 mg) for 40 h in CH_2Cl_2 at room temperature. The title compound **3b** was isolated following silica gel column chromatography (90:8:2 *n*-hex:EtOAc: Et_3N) as white crystals (22.5 mg, 45%).

Table 3, entry 2: Following the general procedure allene **1b** (0.088 mmol, 30 mg) was treated with $AgBF_4$ (0.0088 mmol, 1.7 mg) for 58 h in toluene at room temperature. Title compound **3b** was isolated following silica gel column chromatography (90:8:2 *n*-hex:EtOAc: Et_3N) as white crystals (16.6 mg, 53 %).

R_f (80:20 *n*-hex:EtOAc) = 0.28. mp 66 °C. IR(neat): ν_{max}/cm^{-1} 3040 w, 2923 wm 2362 w, 2172 w, 1335 m, 1442 s, 1095 m, 919 m, 691, s, 645 s. δ_H (500 MHz, $CDCl_3$) 7.69 (d, *J* 8, 2H, Ar*H*), 7.26 (t, *J* 7, Ar*H*), 7.20 (d, *J* 8, Ar*H*), 7.15 (d, *J* 7.5, Ar*H*), 6.42 (d, *J* 16, 1H, ArC*H*CH), 5.92 (dd, *J* 6.5, 16, 1H, ArCHC*H*), 5.73 (d, *J* , 1H, NCHCH$_2$C*H*), 5.62 (d, *J* 18.5, NCH$_2$C*H*), 4.83 (appt, 1H, NC*H*), 4.12 (d, *J* 17, 1H, NC*H*H), 3.56 (d, *J* 17.5, 1H, NCH*H*), 2.54 (d, *J* 17.5, 1H, NCHC*H*H), 2.33 (s, 3H, ArCH_3), 2.11 (dd, *J* 3.5, 17, 1H, NCHCH*H*). δ_C (125 MHz, $CDCl_3$) 143.3 (Ar*C*), 136.9 (Ar*C*), 136.6 (Ar*C*), 132.7 (Ar*C*HCH), 129.6 (Ar*C*), 128.6 (Ar*C*), 127.9 (Ar*C*), 127.6 (Ar*C*), 126.5 (Ar*C*), 125.9 (ArCH*C*H), 123.5 (NCHCH$_2$*C*H), 122.9 (NCH$_2$*C*H), 52.5 (N*C*H) , 41.4 (N*C*HH), 30.1 (NCH*C*HH), 21.5 (Ar*C*H_3). *m/z* (HRESI-MS) 362.1191 $C_{20}H_{21}NSO_2Na$ [M + Na]$^+$; 362.1191, required.

2-Methyl-2-phenyl-1-(4-methyl-N-*benzenesulfonamide)-1,2,3,6-tetrahydropyridine* (**3c**)

Table 3, entry 4: Following the general procedure, allene **1c** (0.092 mmol, 30 mg) was treated with $AgBF_4$ (0.0092 mmol, 1.8 mg) for 46 h in CH_2Cl_2 at room temperature. The title compound **3c** was isolated following silica gel column chromatography (90:8:2 *n*-hex:EtOAc: Et_3N) as white crystals (7.6 mg, 25%).

Table 3, entry 5: Following the general procedure, allene **1c** (0.092 mmol, 30 mg) was treated with $AgBF_4$ (0.0092 mmol, 1.8 mg) for 96 h in toluene at 60 ℃. Title compound **3b** was isolated following silica gel column chromatography (90:8:2 *n*-hex:EtOAc: Et_3N) as white crystals (12.5 mg, 42%).

R_f (80:20 *n*-hex:EtOAc) = 0.41. mp 109 °C. IR(neat): ν_{max}/cm^{-1} 3284 w, 2850 w, 2362 w, 2169 w, 1443 m, 1320 m, 1151 s, 1085 s, 689 s, 662 s. δ_H (500 MHz, $CDCl_3$) 7.76 (d, *J* 8.0, 2H, Ar*H*), 7.42 (d, *J* 8.0, 2H, Ar*H*), 7.31-7.23 (m, 5H, Ar*H*), 5.75 (s, 1H, NCH_2CHCH), 5.54 (d, *J* 10.0, 1H, NCH_2CH), 4.52 (d, *J* 19.0, 2H, NC*H*H), 3.29 (d, *J* 19.0, 2H, NCH*H*), 2.60 (dd, *J* 3.0, 18.0, 2H, NCC*H*H), 2.43 (s, 3H, $ArCH_3$), 2.20 (d, *J* 18.5, 2H, NCCH*H*), 1.61 (s, 3H, CH_3). δ_C (125 MHz, $CDCl_3$) 144.5 (Ar*C*), 143.0 (Ar*C*), 140.9 (Ar*C*), 129.6 (Ar*C*), 128.4 (Ar*C*), 127.2 (Ar*C*), 127.0 (Ar*C*), 126.1 (Ar*C*), 125.1 (NCH_2CH), 124.4 ($NCCH_2CH$), 62.3 (N*C*), 46.0 (NCH_2), 34.1 ($NCCH_2$), 31.3 ($NCCH_3$), 21.7 ($ArCH_3$). *m/z* (HRESI-MS) 350.1199 $C_{19}H_{21}NSO_2Na$ $[M + Na]^+$; 350.1191, required.

3-Phenyl-1-(4-methyl-N-*benzenesulfonamide)-1,2,3,6-tetrahydropyridine* (**3d**)

Table 3, entry 7: Following the general procedure, allene **1d** (0.048 mmol, 15 mg) was treated with $AgBF_4$ (0.0048 mmol, 0.9 mg) for 20 h in 1,2-dichloroethane at reflux temperature. Title compound **3d** was isolated following silica gel column chromatography (95:5 *n*-hex:EtOAc) as a brown oil (2.3 mg, 15%).

R_f (90:10 *n*-hex:EtOAc) = 0.24. IR(neat): ν_{max}/cm^{-1} 2920 w, 2850 w, 1597 w, 1346 m, 1162 s, 942 m, 682 m, 652 m. δ_H (500 MHz, $CDCl_3$) 7.63 (d, *J* 8.3, 2H, Ar*H*), 7.31-7.28 (m, 5H, Ar*H*), 7.18 (d, *J* 8.4, 2H, Ar*H*), 5.83 (s, 2H, NCH_2CH and NCH_2CHCH), 3.92 (dd, *J* 1.0, 15.0, 1H, NC*H*HCH=CH), 3.78 (dd, *J* 5.6, 11.6, 1H, NC*H*HCHAr), 3.69-3.66 (m, 1H, C*H*Ar), 3.39 (dd, *J* 3.4, 16.5 , 1H, NCH*H*CH=CH), 2.61 (dd, *J* 8.5, 11.5, 1H, NCH*H*CHAr), 2.41 (s, 3H, $ArCH_3$). δ_C (125 MHz, $CDCl_3$) 143.7 (Ar*C*), 141.5 (Ar*C*), 133.4 (Ar*C*), 129.8 (Ar*C*), 129.1 (Olefinic), 128.8 (Ar*C*H), 128.1 (Ar*C*), 127.8 (Ar*C*), 127.3 (Ar*C*), 123.6 (olefinic), 50.3 (NCH_2CHAr), 44.8 (NCH_2CHCH), 41.9 (Ar*C*H), 21.7 ($ArCH_3$). *m/z* (HRESI-MS) 336.1028 $C_{18}H_{19}NSO_2Na$ $[M + Na]^+$; 336.1027, required.

Table 2, entry 3:

Following the general procedure for silver catalyzed cyclisation, allene **1a** (0.096 mmol, 30 mg) was treated with Ag_2O (0.096 mmol, 2.3 mg) in acetone (1 mL) at room temperature for 28 h. The title compounds **2a** and **2a'** were isolated following silica gel column chromatography (90:8:2 *n*-hex:EtOAc:Et_3N) as white crystals in 61% yield in a ratio of 1:2.8 of **2a** : **2a'**.

Table 2, entry 4:

To an oven dried round bottom flask was added allene **1a** (0.096 mmol, 30 mg, 1 equiv) and the system was purged with N_2 three times. To another oven dried flask was added KO^{t}Bu (0.115 mmol, 12.9 mg, 1.2 equiv) in anhydrous THF (1 mL) and was syringed into the allene flask. The solution was stirred at room temperature for 3 days, 40 °C for 5 h and at reflux temperature for 56 h. The solution was then quenched with NH_4Cl (10 mL), extracted with CH_2Cl_2 (3 x 10 mL), NaCl sat. solution (10 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Following silica gel column chromatography (90:8:2 PE: EtOAc: Et_3N) 17.3 mg (58%) of the title compound **2a** and **2a'** were isolated as white crystals in a ratio of 4:1.

General procedure for Gold catalysed Cyclisation reactions of allenes

To an oven dried round bottom flask was added allene **1a** (0.096 mmol, 30 mg, 1 equiv) and the system was purged with N_2 three times in the dark. In a separate oven dried round bottom flask was added $AgBF_4$ (0.0097 mmol, 1.9 mg, 0.1 equiv) and $(PPh_3)AuCl$ (0.0097 mmol, 4.7 mg, 0.1 equiv) before being dissolved in CH_2Cl_2 (1 mL) in the dark. This solution was then added to the flask containing the allene via syringe at room temperature. The reaction mixture was stirred until TLC analysis indicated consumption of starting material before passing through a short plug of silica gel with washing with EtOAc. The title compounds **2a** and **2a'** were then purified by silica gel column chromatography (80:18:2 PE:EtOAc:Et_3N) as white crystals (16.6 mg, 55%). Any methyl ketone side products were isolated from the same column.

5-Methyl-2-phenyl-1-(4-methyl-N-*benzenesulfonamide)-2,3-dihydro-1*H-*pyrrole* (**2a**) and *2-methylene-5-phenyl-1-(4-methyl*-N- *benzenesulfonamide)pyrrolidine* (**2a'**)

Following the general method starting with allene **1a** (0.096 mmol, 30 mg) was treated with $(PPh_3)AuCl$ (0.0097 mmol, 4.7 mg) and $AgBF_4$ (0.0097 mmol, 1.9 mg) and stirred at room temperature for 46 h. The title compounds could not be separated by silica gel column chromatography (80:18:2 PE:EtOAc:Et_3N) and isolated as white crystals (16.6 mg, 55%).

R_f (80:20 PE:EtOAc) = 0.41. mp 124 °C. IR(neat): ν_{max}/cm^{-1} 3031 w, 2969 w, 1340 m, 1160 s, 1096 s, 712 s, 699 s, 656 s. δ_H (500 MHz, $CDCl_3$) δ = 7.66 (d, *J* 8.5, 2H, Ar*H*), 7.35-7.30 (m, 5H, Ar*H*), 7.28-7.24 (m, 2H, Ar*H*) for both **2a** and **2a'. 2a:** δ = 5.13 (d, *J* 3.0, 1H, NC*H*), 4.89 (s, 1H, NC=C*H*), 2.67 (app t, *J* 10.5, 1H, NCHC*H*H), 2.43 (s, 3H, Ts-CH_3), 2.19 (d, *J* 16.5, 1H, NCHCH*H*), 2.17 (s, 3H, CCH_3). **2a':** δ = 5.21 (dd, *J* 3.5, 8.0 Hz, 1H, NC*H*), 5.15 (s, 1H, C=C*H*H), 4.43 (s, 1H, C=CH*H*), 2.57-2.52 (m, 1H, H_2C=CC*H*H), 2.43 (s, 3H, Ts-CH_3), 2.31-2.28 (m, 1H, H_2C=CCH*H*), 2.03-2.11 (m, 1H, NHCHC*H*H), 1.76-1.75 (m, 1H, NHCHCH*H*). δ_C (125 MHz, $CDCl_3$) 145.3 (Ar*C*), 143.9 (Ar*C*), 143.8 (Ar*C*), 143.6 (Ar*C*), 142.7 (Ar*C*), 139.8 (Ar*C*), 136.1 (Ar*C*), 129.8 (Ar*C*), 129.5 (Ar*C*), 128.7 (Ar*C*), 128.6 (Ar*C*), 127.7 (Ar*C*), 127.5 (Ar*C*), 126.1 (Ar*C*), 126.0 (Ar*C*). **2a:** δ = 110.9 (C=*C*H), 65.0 (N*C*H), 37.4 ($NCHCH_2$), 21.7 (CH_3), 16.0 ($NCCH_3$). **2a':** δ = 91.6 ($NCCH_2$), 66.9 (N*C*H), 32.4 ($NCHCH_2$), 31.1 ($NCHCH_2CH_2$), 21.7 (CH_3). *m/z* (HRESI-MS) 314.1215 $C_{18}H_{20}NSO_2Na$ $[M + H]^+$; 314.1238, required.

*(*E*)-5-Methyl-2-styryl-1-(4-methyl*-N-*benzenesulfonamide)-2,3-dihydro-1*H-*pyrrole* (**2b)** and *(*E*)-2-methylene-5-styryl-1-(4-methyl*-N-*benzenesulfonamide)pyrrolidine* **(2b')**

Following the general procedure, allene **1b** (0.10 mmol, 35 mg) was treated with $(PPh_3)AuCl$ (0.01 mmol, 4.9 mg) and $AgBF_4$ (0.01 mmol, 1.9 mg) for 1.5 h before filtering through a silica plug and washing with EtOAc. The title compound **2b** was isolated as a white/yellow solid (8.4 mg, 24% yield) following silica gel column chromatography (90:8:2 *n*-hex:EtOAc:Et_3N).

R_f (80:20 *n*-hex:EtOAc) = 0.39. mp 117 °C IR(neat): ν_{max}/cm^{-1} 2923 w, 2710 w, 1710 m, 1596 w, 1419 m, 1321 m, 1152 s, 1091 m, 971 m, 815 m, 667 s. δ_H (500 MHz, $CDCl_3$) 7.71 (d, *J*

7.5, 2H, Ar*H*), 7.38 (d, *J* 7.5, Ar*H*), 7.31-7.22 (m, 5H, Ar*H*), 6.64 (d, *J* 16, 1H, ArC*H*CH), 6.19 (dd, *J* 6.5, 15.5, 1H, ArCHC*H*), 4.90 (s, 1H, CC*H*), 4.77 (appt, *J* = 7 Hz, NC*H*), 2.42 (s, 5H, TsCH_3 + NCHCH*H*), 2.12 (s, 1H,CH_3), 2.06 (appd, *J* 16.5, 2H, NCHC*H*H). δ_C (125 MHz, $CDCl_3$) 143.6 (Ar*C*), 139.4 (Ar*C*), 136.8 (Ar*C*), 136.2 (Ar*C*), 130.3 (Ar*C*HCH), 129.8 (ArCH*C*H), 128.6 (Ar*C*), 127.8 (Ar*C*), 127.5 (Ar*C*), 126.8 (Ar*C*), 126.5 (Ar*C*), 111.2 (NCHCHH*C*H), 63.9 (N*C*H), 34.7 (NCH*C*HH), 21.7 (Ar*C*H_3), 16.0 (*C*H_3).*m/z* (HRESI-MS) 362.1203 $C_{20}H_{21}NSO_2Na$ $[M + Na]^+$; 362.1191, required.

2,5-Dimethyl-2-phenyl-1-(4-methyl-N-*benzenesulfonamide)-2,3-dihydro-1*H*-pyrrole* (**2c**) and *2-methyl-5-methylene-2-phenyl-1-(4-methyl*-N-*benzenesulfonamide)pyrrolidine* (**2c'**)

Following the general procedure, allene **1c** (0.11 mmol, 35 mg) was treated with $(PPh_3)AuCl$ (0.011 mmol, 5.4 mg) and $AgBF_4$ (0.011 mmol, 2.1 mg) for 2.5 h before filtering through a silica plug with washing with EtOAc. The title compound **2c** was isolated as a yellow/brown oil (4.1 mg, 12 % yield) following silica gel column chromatography (90:8:2 *n*-hex:EtOAc:Et_3N).

R_f (80:20 *n*-hex:EtOAc) = 0.40. mp 117 °C. IR(neat): ν_{max}/cm^{-1} 2927 w, 1726 w, 1599 w, 1495 w, 1447 w, 1343 m, 1157 s, 1092 s, 698 m, 674 s. δ_H (500 MHz, $CDCl_3$) 7.43 (d, *J* 8.5, 2H, Ar*H*), 7.38 (d, *J* 8.5, Ar*H*), 7.28-7.22 (m, 3H, Ar*H*), 7.14 (d, *J* 8.0, 2H, Ar*H*), 4.74 (s, 1H, CH_3CCH), 2.82 (d, *J* 16.5, 1H, NCCH*H*), 2.67 (d, *J* 16.5, 1H, NCC*H*H), 2.38 (s, 3H, ArCH_3), 2.10 (s, 3H, HCCH_3), 2.01 (s, 3H, NCCH_3). δ_C (125 MHz, $CDCl_3$) 146.6 (Ar*C*), 142.7 (Ar*C*), 140.5 (Ar*C*), 139.4 (HC*C*CH3), 129.4 (Ar*C*), 128.2 (Ar*C*)127.1 (Ar*C*), 126.0 (Ar*C*), 104.3 (CH_3CCH), 72.6 (N*C*CH_3), 48.9 (NC*C*H_2), 27.0 (NC*C*H_3), 21.6 (Ar*C*H_3), 16.2 (HCC*C*H_3). *m/z* (HRESI-MS) 328.1384; 328.1371, required.

Isolation of methyl ketone side products by silica gel column chromatography

4-Methyl-N-*(4-oxo-1-phenylpentyl)benzenesulfonamide* (**4a**)

Isolated following silica gel column chromatography as white crystals. The % conversions were determined from ^{1}H NMR analysis of the crude reaction materials (see footnotes in Tables 1-3 for specific details).

R_f (80:20 PE:EtOAc) = 0.08. mp 114 °C. IR(neat): ν_{max}/cm^{-1} 3253 m, 2924 w, 1691 m, 1156 s, 663 s. δ_H (500 MHz, $CDCl_3$) 7.52 (d, *J* 8.0, 2H, Ar*H*), 7.14-7.0 (m, 7H Ar*H*), 5.35 (m, 1H, N*H*), 4.28 (app q, *J* 7.0, 1H NHC*H*), 2.49 (m, 2H, CHCH_2), 2.34 (s, 3H, Ts-CH_3), 2.10 (s, 3H, COCH_3), 1.97 (m, 2H, COCH_2). δ_C (125 MHz, $CDCl_3$) 208.6 (CH_2CO), 143.1 (Ar*C*), 140.8 (Ar*C*), 137.8 (Ar*C*), 129.4 (Ar*C*), 128.6 (Ar*C*), 127.5 (Ar*C*), 127.1 (Ar*C*), 126.4 (Ar*C*), 57.8 (NH*C*H), 40.0 (CO*C*H_2), 31.1 (NHCH*C*H_2), 30.2 (CO*C*H_3), 21.5 (Ts-*C*H_3). *m/z* (HRESI-MS) 354.1124 $C_{18}H_{21}NSO_3Na$ $[M + H]^+$; 354.1140, required.

(E)-*4-Methyl*-N-*(6-oxo-1-phenylhept-1-en-3-yl)benzenesulfonamide* (**4b**)

Isolated following silica gel column chromatography as white crystals.

R_f (80:20 *n*-hex:EtOAc) = 0.11. mp 115 °C. IR(neat): ν_{max}/cm^{-1} 3287 w, 2923 w, 2164 w, 2035 w, 1710 m, 1597 w, 1420 m, 1319 m, 1151 s, 927 m, 817 m, 698 m. δ_H (500 MHz, $CDCl_3$) 7.71 (d, *J* 8.0, 2H, Ar*H*), 7.26-7.19 (m, 5H, Ar*H*), 7.07 (d, *J* 7.0, 2H, Ar*H*), 6.14 (d, *J* 16, 1H, ArC*H*CH), 5.69 (dd, *J* 7.0, 16, 1H, ArCHC*H*), 4.74 (d, *J* 8.0, 1H, N*H*), 3.92 (quint, *J* 7.0, 1H, NHC*H*), 2.62-2.55 (m, 2H, CH_3COCH_2), 2.31 (s, 3H, ArCH_3), 2.13 (s, 3H, CH_3), 1.88-1.79 (m, 2H, NHCHCH_2). δ_C (125 MHz, $CDCl_3$) 208.5 (*C*O), 143.5 (Ar*C*), 138.2 (Ar*C*), 136.2 (Ar*C*), 131.7 (Ar*C*HCH), 129.7 (Ar*C*), 128.6 (Ar*C*), 128.5 (ArCH*C*H), 128.0 (Ar*C*), 127.4 (Ar*C*), 126.5 (Ar*C*), 55.9 (NH*C*H), 39.6 (CH_3COCH_2), 30.3 (*C*H_3), 29.3 (NHCH*C*H_2), 21.5 (Ar*C*H_3). *m/z* (HRESI-MS) 380.1303 $C_{20}H_{23}NSO_3Na$ $[M + Na]^+$; 380.1296, required.

4-Methyl-N-*(2-methyl-6-oxoheptan-3-yl)benzenesulfonamide* (**4e**)

Isolated following silica gel column chromatography as white crystals.

R_f (80:20 *n*-hex:EtOAc) = 0.12. mp 85 °C. IR(neat): ν_{max}/cm^{-1} 3040 w, 2923 wm 2362 w, 2172 w, 1335 m, 1442 s, 1095 m, 919 m, 691, s, 645 s. δ_H (500 MHz, $CDCl_3$) 7.72 (d, *J* 8.0, 2H, Ar*H*), 7.29 (d, *J* 8.0, Ar*H*), 4.50 (s, 1H, N*H*), 3.13-3.08 (m, 1H, NHC*H*), 2.53 (dt, *J* 18.5, 7.0, 1H, CH_3COCHH), 2.42-2.35 (m, 4H, ArCH_3 + CH_3COCHH), 2.07 (s, 3H, CH_3), 1.75-1.69 (m, 1H, NHCHCH*H*), 1.64-1.57 (m, 1H, NHCHC*H*), 1.51-1.43 (m, 1H, NHCHC*H*H), 0.76 (d, *J* 6.5, NHCHCH(CH_3)$_2$), 0.72 (d, *J* 7.0, NHCHCH(CH_3)$_2$). δ_C (125 MHz, $CDCl_3$) 209.0 (*C*O), 143.3 (Ar*C*), 138.7 (Ar*C*), 129.7 (Ar*C*), 127.1 (Ar*C*), 59.0 (NH*C*H), 39.9 (CH_3COCH_2), 32.4 (NHCH*C*H), 30.1 (*C*H_3), 24.9 (NHCH*C*H_2), 21.6 (Ar*C*H_3), 18.3 (NHCHCH(*C*H_3)$_2$), 17.9 (NHCHCH(*C*H_3)$_2$). *m/z* (HRESI-MS) 320.1289 $C_{15}H_{23}NSO_3Na$ $[M + Na]^+$; 320.1291 , required.

Supplementary Material

^{1}H NMR and ^{13}C NMR spectra of all new compounds are available on the Journal's website.

Conflicts of Interest

The authors declare no conflicts of interest.

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