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# Gold(III) Chloride/Silver Triflate: A Highly Efficient Catalyst for Ring-Opening Reaction of Aziridines with Electron-Rich Arenes

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**Abstract:** Gold(III) chloride/silver triflate was found to a highly efficient catalyst in the ring-opening of aziridines with electron-rich arenes and the desired β-arylamines were afforded in good to excellent yields under mild reaction conditions.

**Keywords:** arenes; aziridines; gold(III) chloride; ring-opening reaction; silver triflate

## Introduction

Recently, gold catalysis has attracted much attention and has become a hot area in chemistry.[1] The unique activity of gold catalysts has been discovered and demonstrated in many reactions. Among these, it was found that arylgold(III) complexes could be formed from gold(III) chloride with aromatic compounds regiospecifically at room temperature.[2] And also, it was reported that $AuCl_3$ could catalyze the 1,4-addition of electron-rich aromatic rings to methyl vinyl ketone in acetonitrile,[3] the Friedel–Crafts-type addition of arenes to imines,[4] as well as the intramolecular or intermolecular reactions of epoxides with electron-rich arenes.[5a] For these reaction process, although mechanisms have not been confirmed through mechanistic studies, it was proposed that the reaction may involve an auration step followed by an attack of the arylgold(III) to the electrophiles or proceed through a concerted Lewis acid mechanism with gold(III). Prompted by these results, we envisaged that aziridines may also be employed as substrate in the gold(III)-catalyzed reaction of arenes, due to the unique activity of gold catalysts for the functionalization of arenes[4,5] and the structural similarity of epoxides with aziridines (Figure 1).

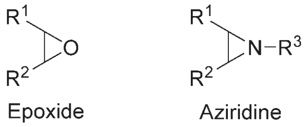
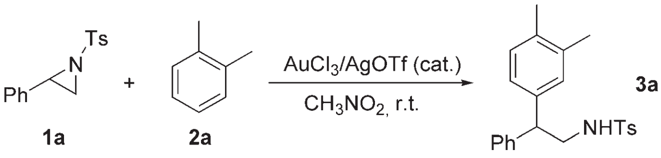


**Figure 1.** Structures of epoxide and aziridine skeletons.

It is well-known that aziridine is a versatile building block for the synthesis of many nitrogen-containing biologically active molecules.[6] Among the procedures of ring opening of aziridines, a nucleophilic ring-opening reaction is one of the major routes to highly functionalized compounds.[6] Although ring-opening reactions of aziridines with various nucleophiles (such as thiols, amines, alcohols, and silylated nucleophiles) have been developed, there are few observations for utilizing arenes as substrates.[7] In 1996, Mann reported $BF_3·OEt_2$ promoted reactions of aziridines with arenes.[7a] However, 1.0 equiv. of $BF_3·OEt_2$ had to be utilized. Indium triflate was also employed for the reaction of aziridines with arenes.[7b] The reaction was usually completed in several hours in the presence of catalytic amount of $In(OTf)_3$ (5–10 mol%) and afforded the product as a mixture of regioisomers in most of cases. In the course of our ongoing studies on novel methods for aziridine transformations,[8] we explored the possibility of gold(III)-catalyzed ring-opening reactions of aziridines with arenes. The results are disclosed herein.

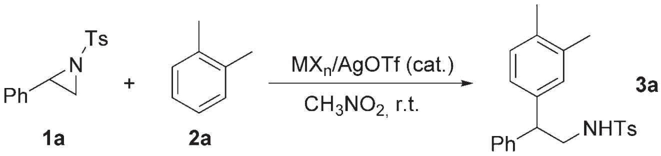
## Results and Discussion

Our studies commenced with the ring-opening reaction of aziridine **1a** with *o*-xylene **2a** in the presence of gold(III) chloride (5 mol%) and silver triflate (15 mol%) in dichloromethane at room temperature. To our delight, we observed the formation of the desired



AgOTf (15 mol %): 65% yield, 4 h
AuCl$_3$ (5 mol %), AgOTf (15 mol %): 82% yield, 2 min
AuCl$_3$ (1 mol %), AgOTf (3 mol %): 80% yield, 2 min

**Scheme 1.** Initial studies for reaction of aziridine **1a** and arene **2a** catalyzed by AuCl$_3$/AgOTf.



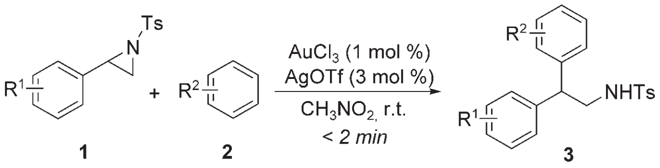
AgOTf (15 mol %): 65% yield, 4 h
BiCl$_3$ (5 mol %), AgOTf (15 mol %): 64% yield, 40 min
YbCl$_3$ (5 mol %), AgOTf (3 mol %): 59% yield, 20 min
ZnCl$_2$ (5 mol %), AgOTf (15 mol %): 66% yield, 5 min
BF$_3$ •OEt$_2$ (5 mol %), AgOTf (15 mol %): 54% yield, 40 min

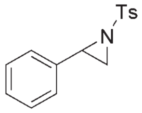
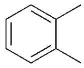
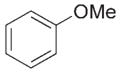
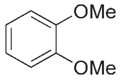
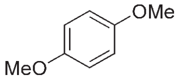
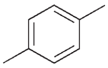
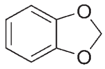
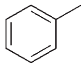
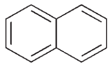
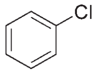
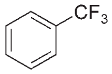
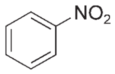
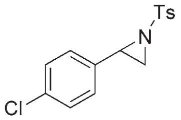
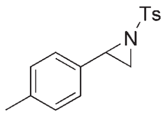
**Scheme 2.** Reaction of aziridine **1a** and arene **2a** catalyzed by other metal salts combined with AgOTf.

product **3a** and a 35% isolated yield of **3a** was obtained after 1 hour. No regioisomer was observed. Further investigation revealed that the yield could be increased to 50% when the reaction was performed in dichloroethane. After screening other solvents (such as THF, ether, CH$_3$NO$_2$), it was found that the reaction was highly efficient and completed in 2 min (82% yield) in anhydrous CH$_3$NO$_2$. (Scheme 1) Decreasing the reaction temperature to 0°C gave similar results and the reaction time was prolonged to 10 min. Without the gold(III) catalyst, silver triflate (15 mol%) could also promote this reaction and 65% of product **3a** was obtained after 4 h. If gold(III) chloride alone was utilized as catalyst, a mixture of β-arylamine **3a** and β-chloroamine was generated (30% yield). No reaction occurred in the absence of catalyst. These results illustrate the high efficiency and importance of combined catalytic system. Moreover, the catalytic loading of gold(III) could be lowered to 1 mol% without loss of efficiency (80% yield, 2 min, Scheme 1). However, 0.1 mol% of AuCl$_3$/AgOTf retarded the reaction since it did not go to completion after 4 days. We also tried other metal salts combined with silver triflate as catalyst instead of gold chloride in the reaction of aziridine **1a** with *o*-xylene **2a** in CH$_3$NO$_2$ at room temperature, and the results were presented in Scheme 2. From Scheme 2, it was found that the addition of other metal salts could accelerate the reaction. For example, as described above, this reaction catalyzed by silver triflate (15 mol%) afforded the desired product **3a** in 65% yield after 4 h. A similar result was generated when BiCl$_3$ (5 mol%) was added in the reaction system, however, the reaction time was shortened to 40 min. A slightly lower yield was observed when YbCl$_3$ (5 mol%) or BF$_3$·OEt$_2$ was employed in the reaction combined with silver triflate. Again, only 20 or 40 min were needed for this transformation. Interestingly, the reaction went to completion in 5 min (66% yield) when zinc chloride (5 mol%) was utilized as catalyst, which showed a similar efficiency as compared with gold chloride. The exact role of the silver salt is not clear although it seems that the silver cation may be the catalytically active center. From these observations, as well as the possible pathway proposed by He,[5] it might also help to remove the chloride anion from AuCl$_3$ to generate a more electrophilic gold(III) species although silver triflate alone did catalyze the reaction under the same conditions as described above. The results also indicated this reaction may involve a Friedel–Crafts-type addition process,[9] presumably through generation of a benzyl carbon cation from 2-phenylaziridine **1a** which attacks the benzene ring.

To demonstrate the generality of this method, we next investigated the scope of this reaction under the optimized conditions [CH$_3$NO$_2$, AuCl$_3$ (1 mol%)/AgOTf (3 mol%), room temperature] and the results are summarized in Table 1. As shown in Table 1, this method is equally effective for both aziridines and electron-rich arenes and the catalyst showed high efficiency in this reaction. All reactions with electron-rich arenes were finished in 2 min and good to excellent isolated yields of corresponding products were obtained, although in some cases 2 mol% or 5 mol% of catalyst were used. For example, 2 mol% of catalyst had to be used in the reaction of *N*-tosyl-2-phenylaziridne **1a** with *p*-xylene **2e** in order to obtain a respectable yield in 2 min (entry 5). Furthermore, under these catalytic conditions, regiospecificity was observed for all electron-rich arenes employed. In contrast to a previous report,[7] the only isomer obtained was that from attack on the benzylic position of the aziridine. However, electron-deficient arenes were not good partners for this kind of transformation. When chlorobenzene, trifluoromethylbenzene, or nitrobenzene was employed as substrate in the reaction of aziridine **1a** catalyzed by AuCl$_3$/3 AgOTf (5 mol%) (entries 9–11), a complicated reaction mixture was observed although aziridine **1a** had disappeared after 5 min. Interestingly, aziridine **1a** reacted with cyanobenzene **2m**, leading to the formation of imidazoline **4** in 35% yield through [3+2]-cycloaddition of aziridine with nitrile [Scheme 3, Eq. (1)].[10] We also tested the reaction of an aziridine without a tosyl group attached on the nitrogen. No reaction occurred when 2-phenylaziridine was employed in the reaction of arene **2c**. Reaction of 1-benzyl-2-phenylaziridine **5**

**Table 1.** $AuCl_3$/AgOTf-catalzyed ring-opening reaction of aziridines with arenes at room temperature.[a]



| Entry | Aziridine | | Arene | | Product | Yield [%][b] |
|---|---|---|---|---|---|---|
| 1 |  | **1a** |  | **2a** | **3a** | 80 |
| 2 | | **1a** |  | **2b** | **3b** | 93 (5.2:1)[e] |
| 3 | | **1a** |  | **2c** | **3c** | 81 |
| 4[c] | | **1a** |  | **2d** | **3d** | 70 |
| 5[c] | | **1a** |  | **2e** | **3e** | 64 |
| 6 | | **1a** |  | **2f** | **3f** | 91 |
| 7[d] | | **1a** |  | **2g** | **3g** | 78 |
| 8[d] | | **1a** |  | **2h** | **3h** | 75 |
| 9[d] | | **1a** |  | **2i** | - | complicated |
| 10[d] | | **1a** |  | **2j** | - | complicated |
| 11[d] | | **1a** |  | **2k** | - | complicated |
| 12 |  | **1b** | | **2c** | **3i** | 95 |
| 13[d] | | **1b** | | **2d** | **3j** | 80 |
| 14 | | **1b** | | **2f** | **3k** | 89 |
| 15 |  | **1c** | | **2c** | **3l** | 87 |
| 16 | | **1c** | | **2d** | **3m** | 70 |

[a] *Reaction conditions:* aziridine **1** (0.50 mmol), arene **2** (0.60 mmol), $AuCl_3$ (1 mol%), AgOTf (3 mol%), $CH_3NO_2$ (2.5 mL), room temperature, 2 min.

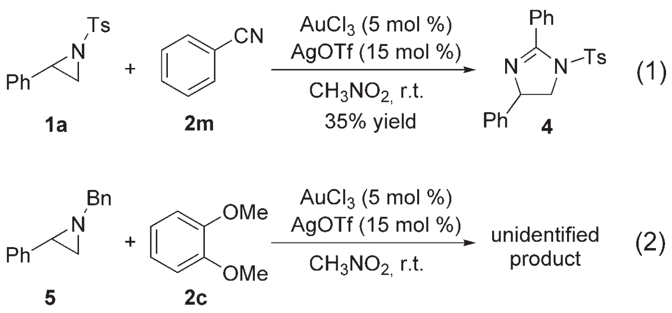
[b] Isolated yield based on aziridine **1**.

[c] $AuCl_3$ (2 mol%), AgOTf (6 mol%).

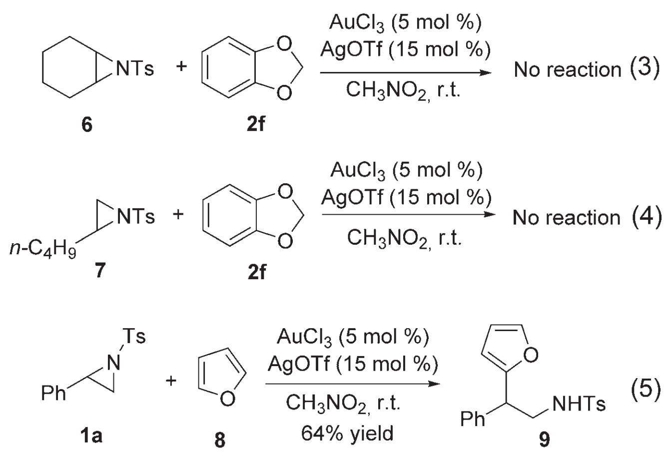
[d] $AuCl_3$ (5 mol%), AgOTf (15 mol%).

[e] Two products were isolated. The major one was *N*-[2-(4-methoxyphenyl)-2-phenylethyl]-4-methylbenzenesulfonamide. The other was *N*-[2-(2-methoxyphenyl)-2-phenylethyl]-4-methylbenzenesulfonamide.

with electron-rich arene **2c** was also tried, as shown in Scheme 3 [Eq. (2)], no desired product was observed and only a small amount of unidentified compound was obtained.



**Scheme 3.** Reaction of aziridine **1a** or **5** with arene **2a** or **2c**.



**Scheme 4.** Other reactions.

Other aziridines were also examined under the conditions shown in Scheme 3. However, no product was detected when aziridine **6** or **7** was utilized as substrate and only starting material was recovered, which was similar to the previous report.[7] [Scheme 4, Eq. (3) and Eq. (4)]. When these two reactions were performed at higher temperature (60 °C), the reaction turned out to be messy. However, reaction of aziridine **1a** with a heterocycle, such as furan **8**, proceeded smoothly under these conditions. [Scheme 4, Eq. (5)]. The reaction was finished in 2 min and the desired product **9** was afforded in 64% yield with excellent regioselectivity. From this case, it was found that the efficiency of this reaction was similar to those with electron-rich arenes.

## Conclusions

In conclusion, we have described a highly efficient and regiospecific ring-opening reaction of aziridine with electron-rich arene catalyzed by gold(III) chloride/silver triflate, which provides a facile and convenient route for the synthesis of β-arylamines. The advantages of this method include: (1) high efficiency and excellent regioselectivity; (2) experimentally operational ease; (3) mild conditions; and (4) low catalytic loading. Efforts to understand the reaction mechanism and explore synthetic utilities of the reactions reported here are in progress in our laboratory.

## Experimental Section

### General Procedure

Under nitrogen atmosphere, aziridine **1** (0.50 mmol) and arene **2** (0.60 mmol) were added subsequently to a mixture of gold(III) chloride (1 mol%) and silver triflate (3 mol%) in anhydrous nitromethane (2.5 mL) at room temperature. After completion of the reaction as indicated by TLC, the reaction mixture was quenched with water (10 mL) and extracted with EtOAc (2 × 10 mL). Evaporation of the solvent followed by purification on silica gel afforded pure product **3**. (All the products are known compounds and the data of products was identical with the literature reports,[7] see Supporting Information.)

### Supporting Information

General experimental information, characterization data, and copies of $^1$H NMR spectra of compounds **3**.

## Acknowledgements

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