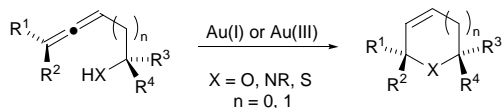


Golden Opportunities in Catalysis

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Introduction

Homogeneous gold catalysis is an emerging area of transition metal catalysis with tremendous potential for the synthesis of complex target molecules.¹ We are particularly interested in the stereoselective synthesis of functionalized allenes and their gold-catalyzed cycloisomerization to chiral heterocycles.



Examples for gold-catalyzed allene cycloisomerizations with high *axis-to-center* chirality transfer:

- α -hydroxyallenes \rightarrow 2,5-dihydrofurans²
- β -hydroxyallenes \rightarrow 5,6-dihydro-2H-pyrans³
- α -aminoallenes \rightarrow 3-pyrrolins⁴
- β -aminoallenes \rightarrow tetrahydropyridins³
- α -thioallenes \rightarrow 2,5-dihydrothiophenes⁵

(first example of a gold-catalyzed C-S bond formation).

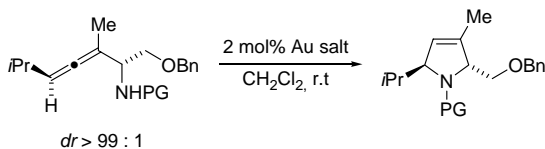
See also: *Tandem* gold/acid-catalyzed cycloisomerization/hydroalkoxylation of homopropargylic alcohols.⁶

Optimization of Chirality Transfer and Catalyst Efficiency

Problem: Decreased chirality transfer in the gold-catalyzed cycloisomerization of protected α -aminoallenes.⁴

Possible Reason: Formation of zwitterionic intermediates which are stabilized by the protecting group.

Solution: Use of unprotected α -aminoallenes and gold(I) instead of gold(III) precatalysts for increased reactivity.⁴



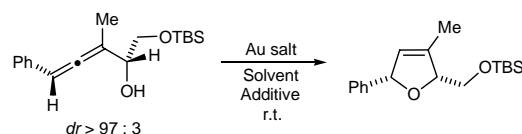
PG	Au salt	Time	Yield	dr
Ms	AuCl ₃	30 min	77%	94 : 6
Ts	AuCl ₃	30 min	93%	95 : 5
Ac	AuCl ₃	30 min	80%	70 : 30
Boc	AuCl ₃	30 min	69%	46 : 54
H	AuCl ₃	5 d	74%	> 99 : 1
H	AuCl	6 h	71%	99 : 1

Problem: Decreased chirality transfer in the gold-catalyzed cycloisomerization of aryl-substituted α -hydroxyallenes.⁷

Possible Reason: Formation of zwitterionic intermediates with a benzyl cation structure.

Solution: Decreasing the Lewis acidity of the gold precatalyst using 2,2'-bipyridine as additive or THF as solvent.⁷

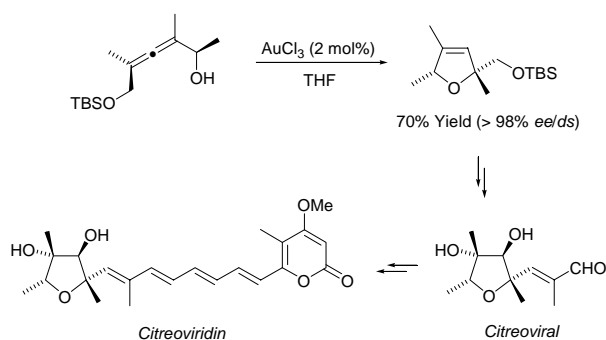
Benefit: Improved stability of the catalyst \rightarrow decrease of the catalyst loading.⁷



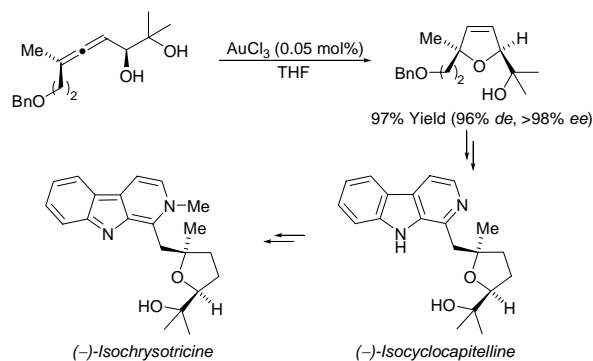
Au salt (mol%)	Additive (mol%)	Solvent	Yield	cis:trans
AuCl ₃ (1)	-	CH ₂ Cl ₂	76%	66 : 34
AuCl (2)	-	CH ₂ Cl ₂	85%	60 : 40
AuCl ₃ (2.5)	2,2'-Bipyridine (5)	CH ₂ Cl ₂	70%	> 97 : 3
AuCl ₃ (2)	-	THF	78%	97 : 3
AuCl ₃ (0.1)	2,2'-Bipyridine (0.2)	THF	92%	85 : 15
AuCl (2.5)	2,2'-Bipyridine (3.8)	CH ₂ Cl ₂	96%	95 : 5

Application in Natural Product Synthesis

Target Molecules: Citreoviral/Citreoviridin:⁸



Target Molecules: (-)-Isocycloapitelline/(-)-Isochrysotricine:⁹



References

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