Cyclization of Gold Acetylides:

Synthesis of Vinyl Sulfonates via Gold Vinylidene Complexes

Janina Bucher, Thomas Wurm, Kumara Swamy Nalivela, Matthias Rudolph, Frank Rominger, and A. Stephen K. Hashmi*

Angew. Chem. Int. Ed., **2014**, DOI: 10.1002/anie.201310280

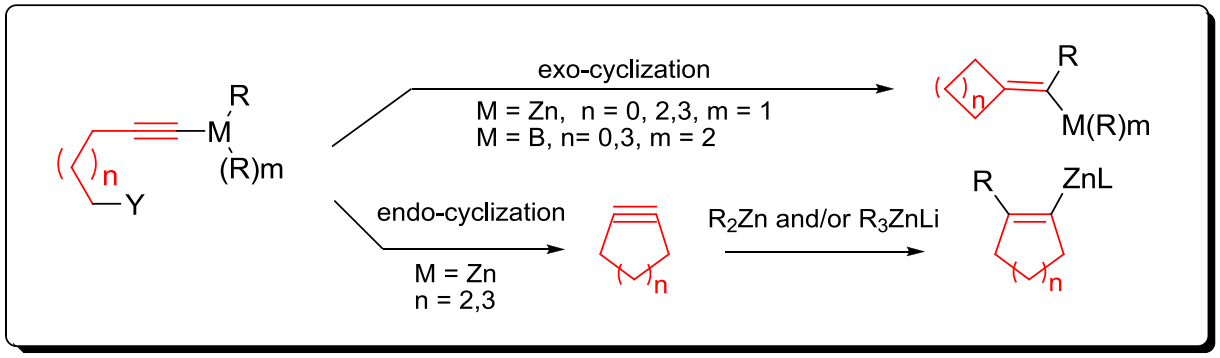
Ophélie Quinonero

Group meeting

10/03/2014

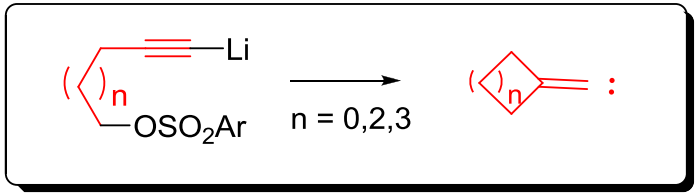
Literature precedents

- Cyclization of alkynyl borate and zincate bearing a leaving group:



Harada *et al. Tet. Lett.* **1997**, 38, 2855-2858

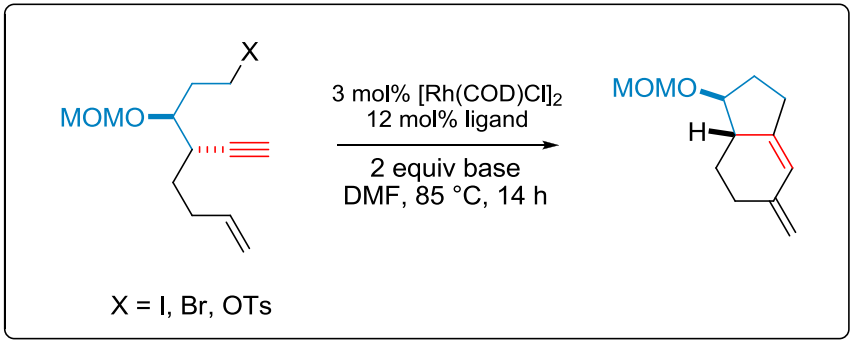
- Cyclization of alkynyl lithium:



Harada *et al. J. Org. Chem.* **1998**, 63, 9007-9012

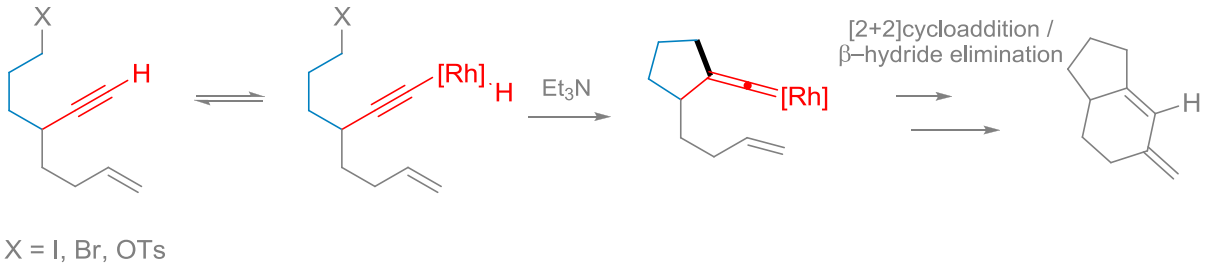
Literature precedents

- Rhodium vinylidene complexe:



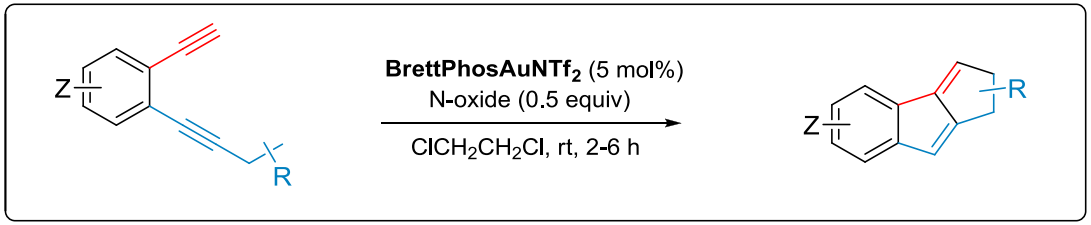
Lee *et al*, *J. Am. Chem. Soc*. **2006**, 128, 14818-14819

- Proposed mechanism



Literature precedents

- Dual gold catalysis :



Zhang *et al, J. Am. Chem. Soc.* **2012**, 134, 31-34

Literature precedents

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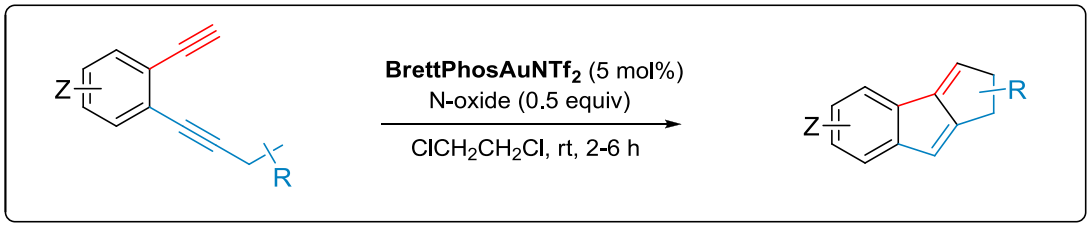

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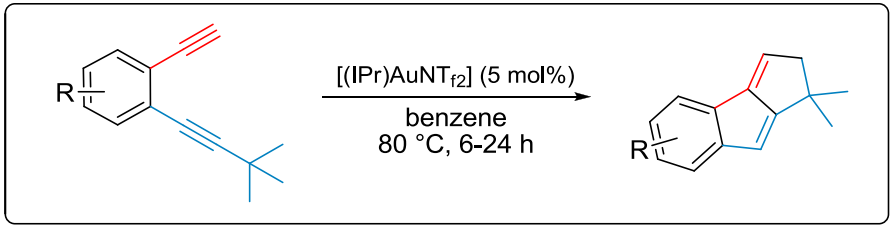

Hashmi *et al*, *Angew. Chem. Int. Ed*. **2012**, 51, 4456-4460

Literature precedents

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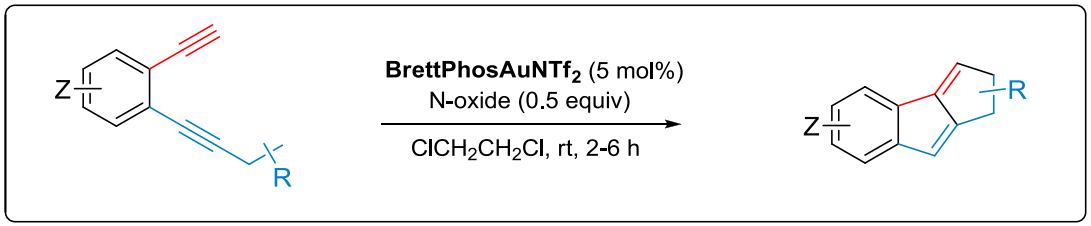

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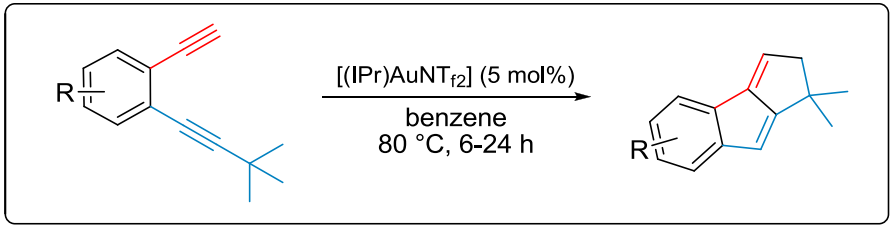

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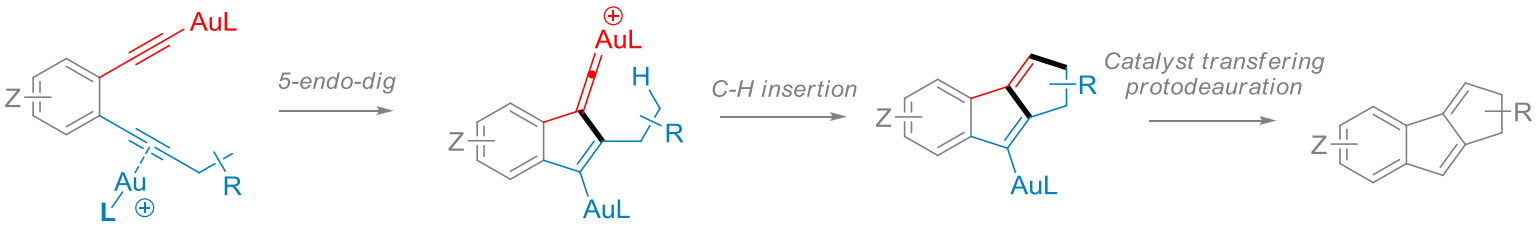
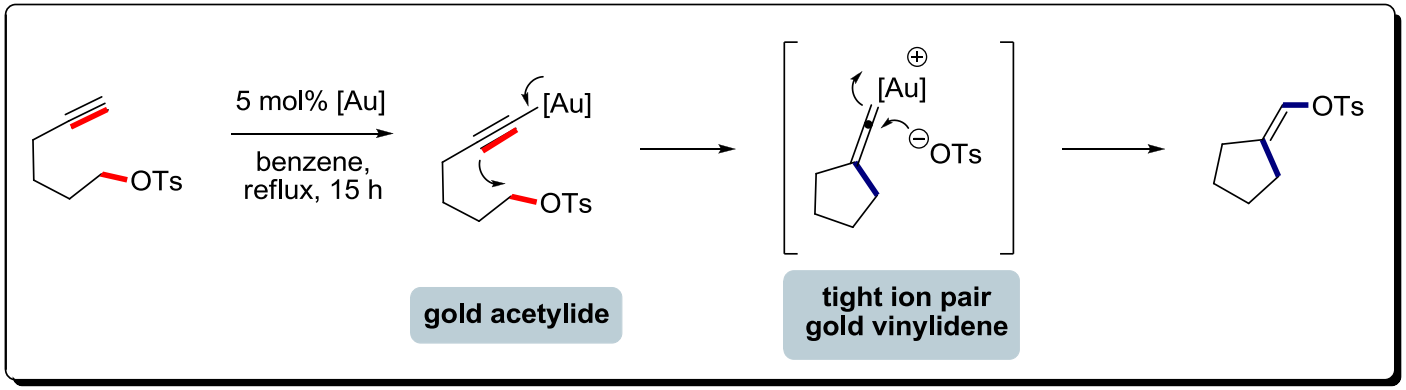
- Proposed mechanism



Leaving Group strategy : a new approach for gold vinylidene synthesis



Cyclization of gold acetylide

↓

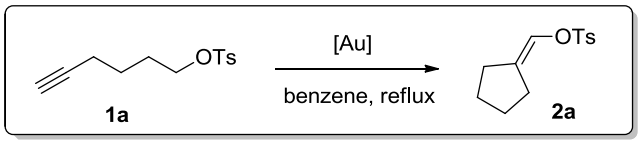
Generation of gold vinylidene intermediate,
via an **unprecedented** non-dual activation mode

↓

Synthesis of useful building blocks
for cross-coupling reaction

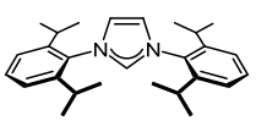
Optimization of the reaction conditions

- Catalyst screening[a]

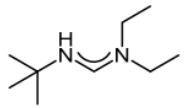


#	catalyst	loading	time	conversion	yield 2a
1	IPrAuOH	5 mol%	16 h	100 %	77 %
2	IPrAuMe	5 mol%	16 h	100 %	74 %
3	IPrAuPh	5 mol%	16 h	100 %	76 %
4	IPrAuPropyne	5 mol%	16 h	100 %	80 %
5	NACAuPropyne	5 mol%	16 h	8 %	8 %
6	XPhosAuPropyne	5 mol%	16 h	100 %	92 %
7	SPhosAuPropyne	5 mol%	16 h	100 %	91 %
8	XPhosAuPropyne	2.5 mol%	16 h	100 %	79 %
9	SPhosAuPropyne	2.5 mol%	18 h	100 %	72 %
10	$NHC_{(15)}$AuPropyne	2.5 mol%	16 h	100 %	81 %
11	$NHC_{(12)}$AuPropyne	2.5 mol%	16 h	94 %	67 %
12	$NHC_{(15)}$AuPropyne	1 mol%	24 h	70 %	63 %

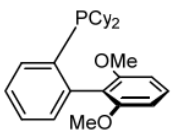
IPr



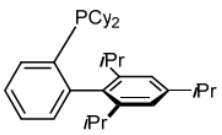
NAC



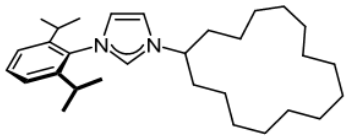
SPhos



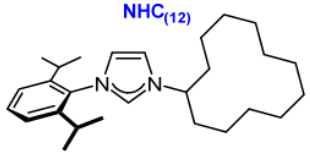
XPhos



$NHC_{(15)}$



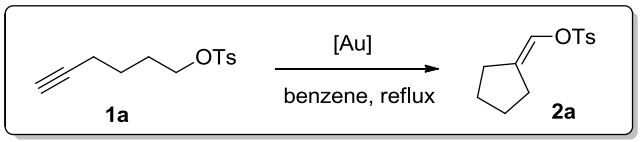
$NHC_{(12)}$



[a] Conversion and Yields determined by GC analysis using cyclooctane as an internal standard

Optimization of the reaction conditions

- Catalyst screening[a]



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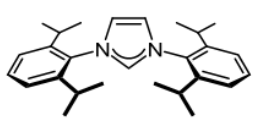
Best « counterion » (X ligand)

IPr



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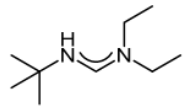

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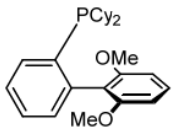

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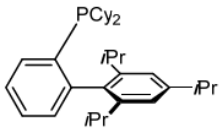

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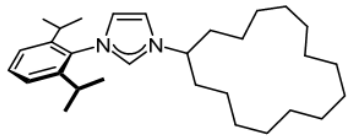

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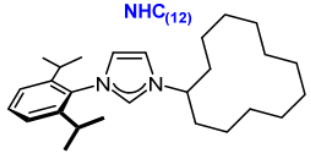

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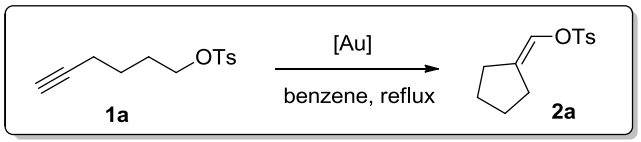

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Best L ligand

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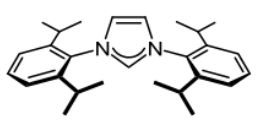

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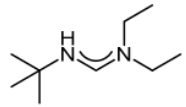

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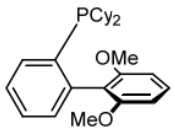

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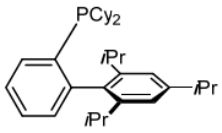

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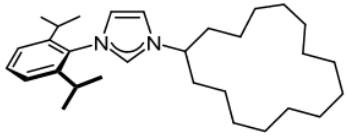

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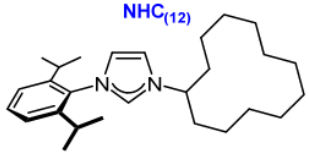
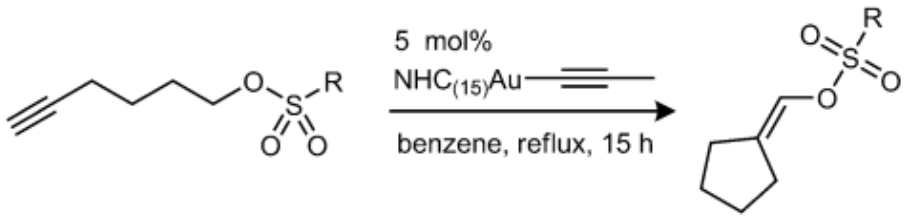


[a] Conversion and Yields determined by GC analysis using cyclooctane as an internal standard

Scope

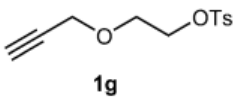
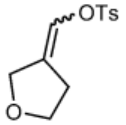
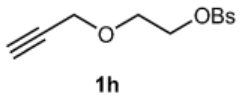
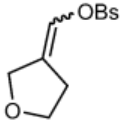
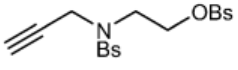
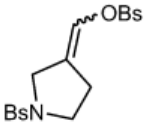
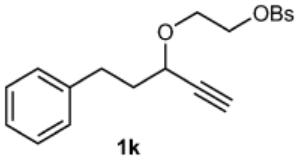
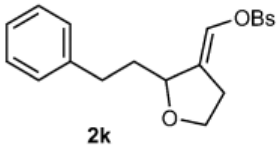
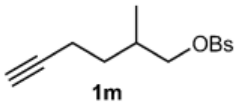
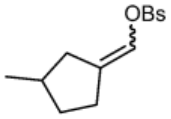


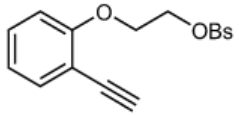
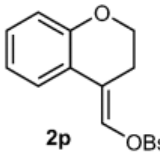
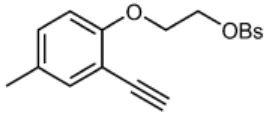
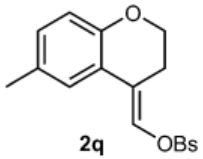
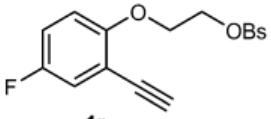
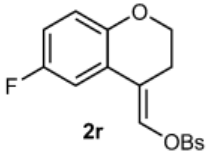
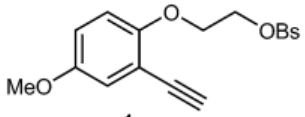
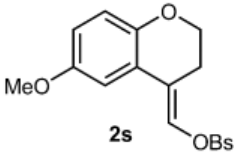
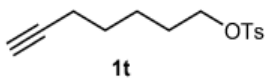
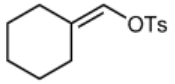
Entry	R	Starting material	Product	Yield [%]
1	*p*-MeC_6H_4	**1a**	**2a**	92
2	*p*-BrC_6H_4	**1b**	**2b**	88
3	*p*-$NO_2C_6H_4$	**1c**	**2c**	53
4	*p*-$MeOC_6H_4$	**1d**	**2d**	84
5	mesityl	**1e**	**2e**	93
6	Me	**1f**	**2f**	72

(All yields refer to isolated products)

- Tolerance for differents sulfonates moieties
- Sulfonates bearing aromatics substituents (good to excellent yields)
- No reaction when replacing sulfonates to halides

Scope

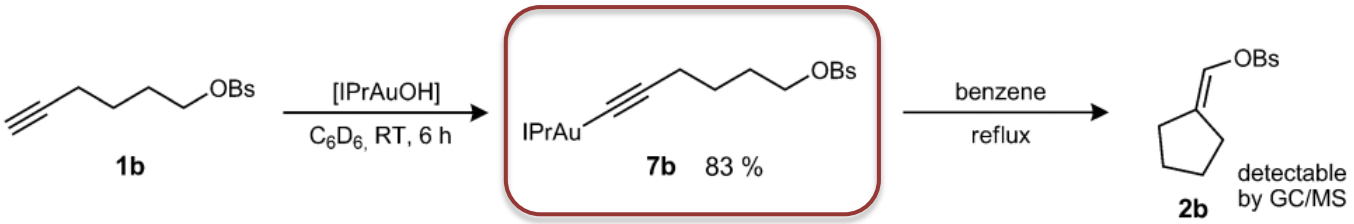
Entry	Starting material	Product	*t*	Yield [%]
1	 **1g**	 **2g**, *E*/*Z* 2.5:1	6 days	21
2	 **1h**	 **2h**, *E*/*Z* 2.5:1	39 h	53
3	 **1j**	 **2j**, *E*/*Z* 4:1	39 h	83
4	 **1k**	 **2k**	15 h	65
5	 **1m**	 **2m**, 2:1	15 h	79

Entry	Starting material	Product	*t*	Yield [%]
6	 **1p**	 **2p**	15 h	82
7	 **1q**	 **2q**	15 h	85
8	 **1r**	 **2r**	48 h	77
9	 **1s**	 **2s**	15 h	78
10	 **1t**	 **2t**	87 h	49

(All yields refer to isolated products)

Mechanistic studies

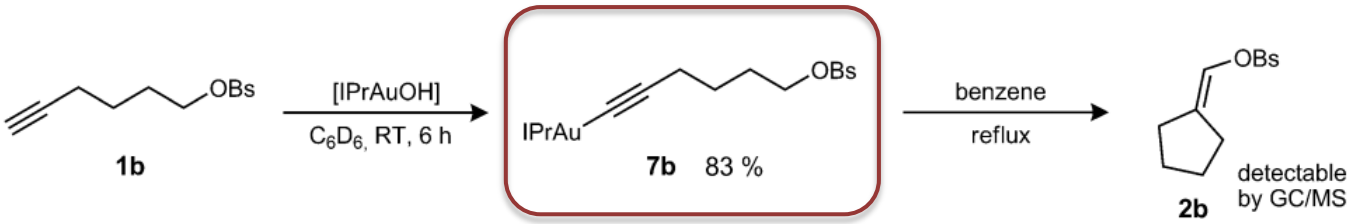
- **Isolation of catalytic intermediate under stoechiometric conditions**



Relevant intermediate

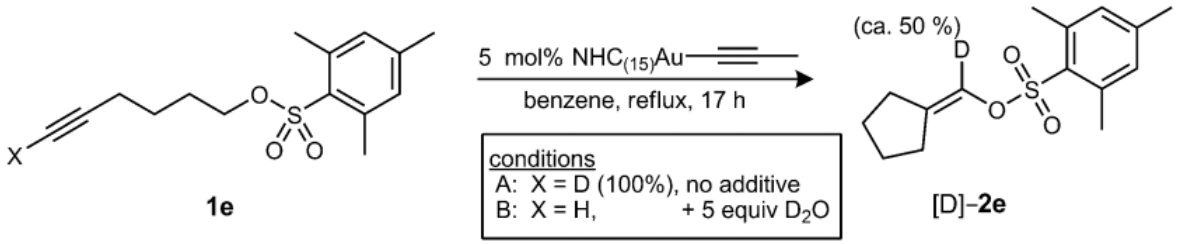
Mechanistic studies

- **Isolation of catalytic intermediate under stoechiometric conditions**



Relevant intermediate

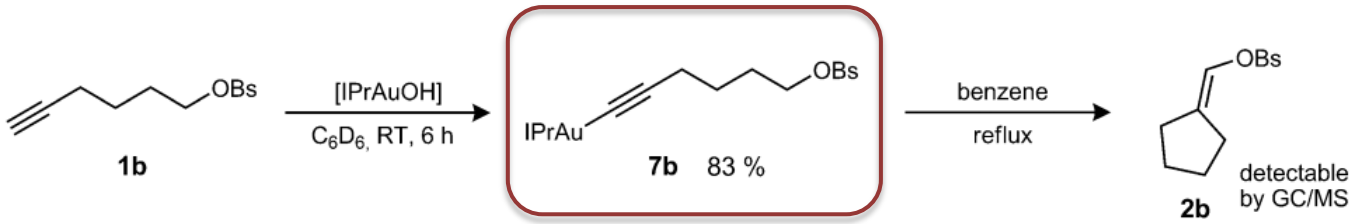
- **Labeling experiments**



→ Highlight of a competition reaction for protodeauration between traces water and SM (catalyst transfer)

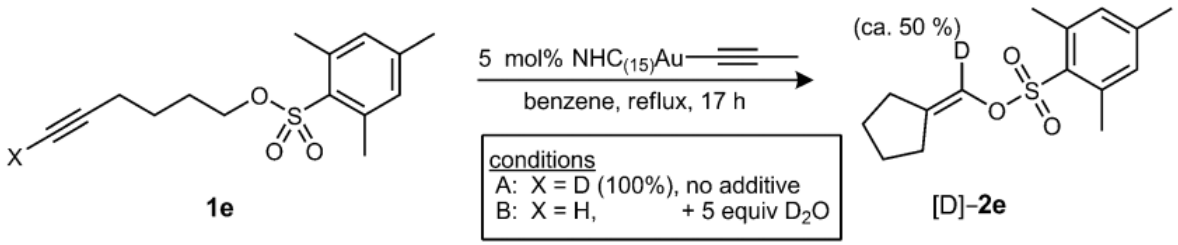
Mechanistic studies

- **Isolation of catalytic intermediate under stoechiometric conditions**



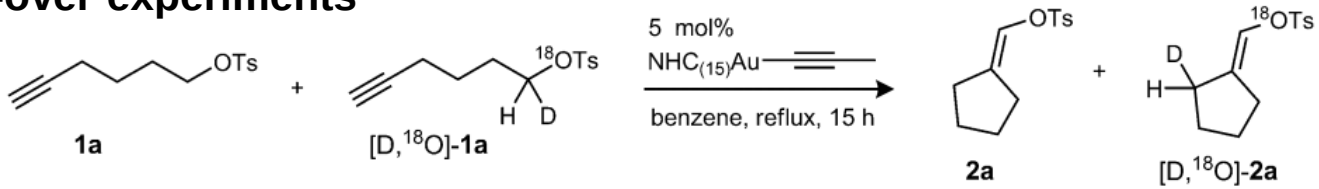
Relevant intermediate

- **Labeling experiments**



→ Highlight of a competition reaction for protodeauration between traces water and SM (catalyst transfer)

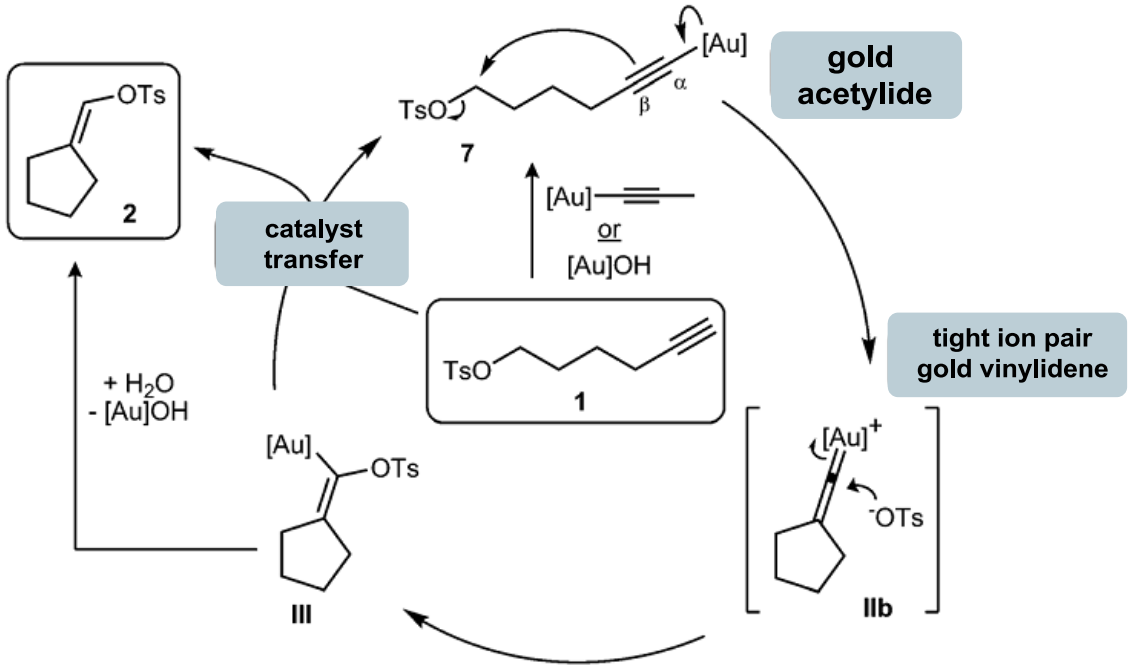
- **Cross-over experiments**



→ Tosylate counterion remains in the gold coordination sphere (tight ion pair or covalently bound) during the catalytic cycle

no cross-over products could be detected

Proposed reaction mechanism



1) Formation of gold acetylide

2) Formation of gold vinylidene

3) Inner sphere tosylate addition to the gold vinylidene

4) Protodeauration of vinylgold species

Conclusion

- **First example** of gold vinylidene synthesis by gold acetylides cyclization **without dual activation mode.**
- A range of **differently substituted sulfonates** can be used.
- **Products** could be further functionnalized by cross coupling reactions and lead to **useful building blocks.**