

Silver-free gold(I) catalysis

Na[Me₃NB₁₂Cl₁₁] as *in situ* activator of ligated gold(I) chlorides^[1]

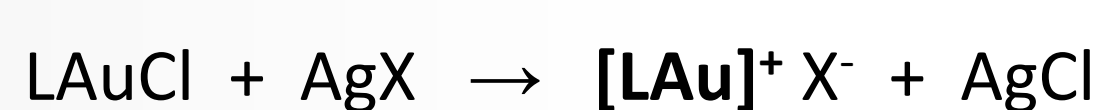
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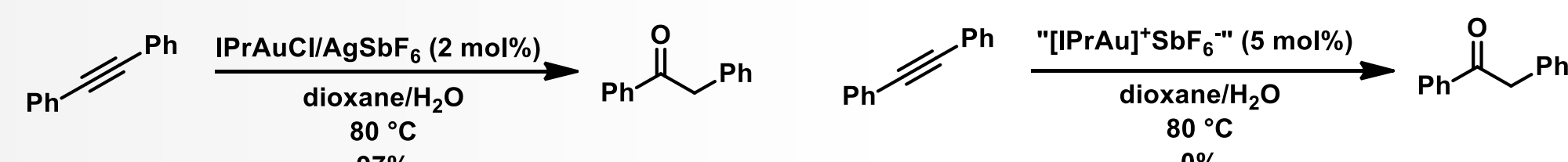
General application

The trouble with silver ...

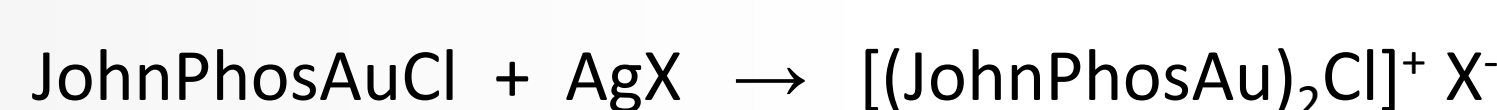
The most common way to generate catalytically active species from gold(I) chloride precatalysts (which are oftentimes commercially available or easily prepared) is by conversion with the silver(I) salt of weakly coordinating anions, which results in the formation of cationic gold(I) and the precipitation of AgCl:



Recent investigations revealed serious complications that go along with this method of activation. Notably, reactivity differs greatly in many transformations depending on whether the catalytic species is formed in the presence of the substrate, or in its absence followed by filtration to remove AgCl:^[2]



A possible explanation for some of these results is the formation of less reactive bridged digold-complexes in the absence of a substrate or coordinating solvent:^[3]



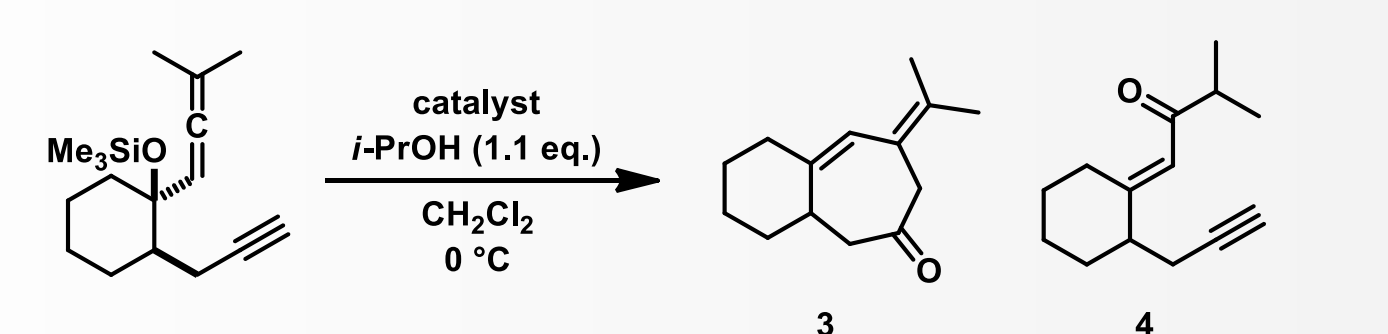
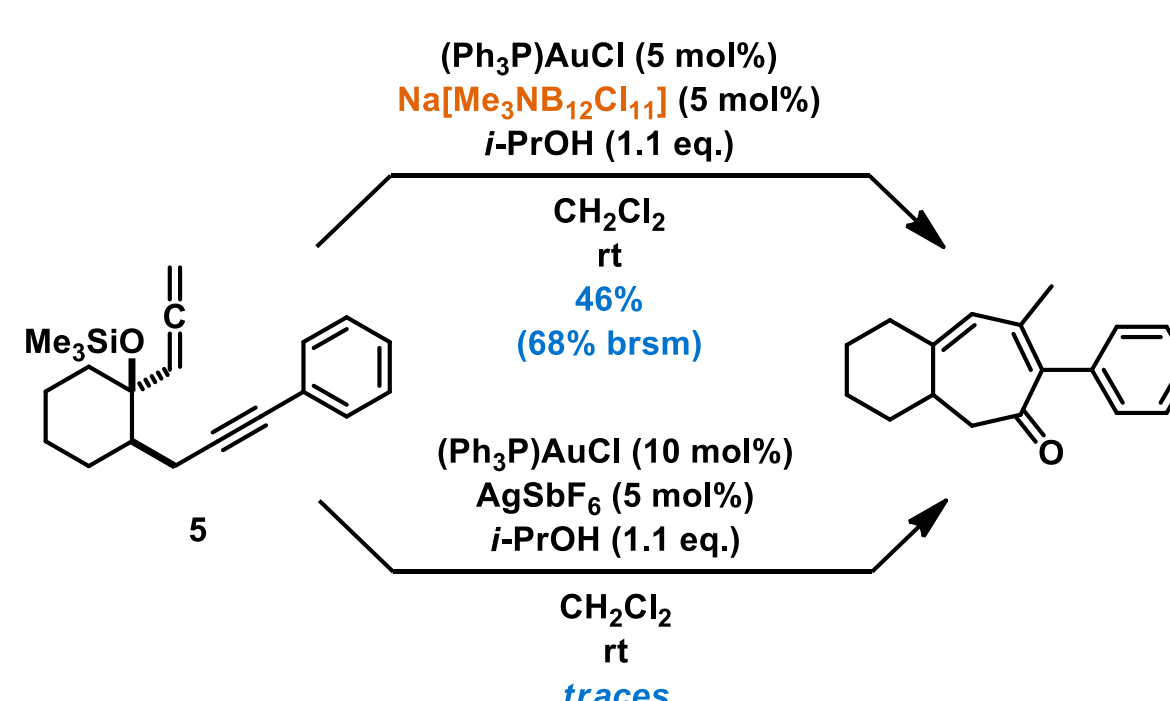
Finding methods or reagents that circumvent these issues by dispensing with silver altogether is therefore of great interest.

A cascade reaction of allenynes

Optimization of reaction conditions

Investigating the reactivity of 5-siloxy-1,6-allenynes, we found that in the presence of (Ph₃P)AuCl and AgSbF₆ a mixture of cycloheptanone **3** and undesired rearrangement product **4** is formed. Preactivation of the catalyst followed by filtration over Celite to remove the silver resulted in the sole formation of **3**. To our delight, the same result was obtained using Na[Me₃NB₁₂Cl₁₁] without filtration, which also proved superior to the silver-free alternative of NaBAR^F₄.

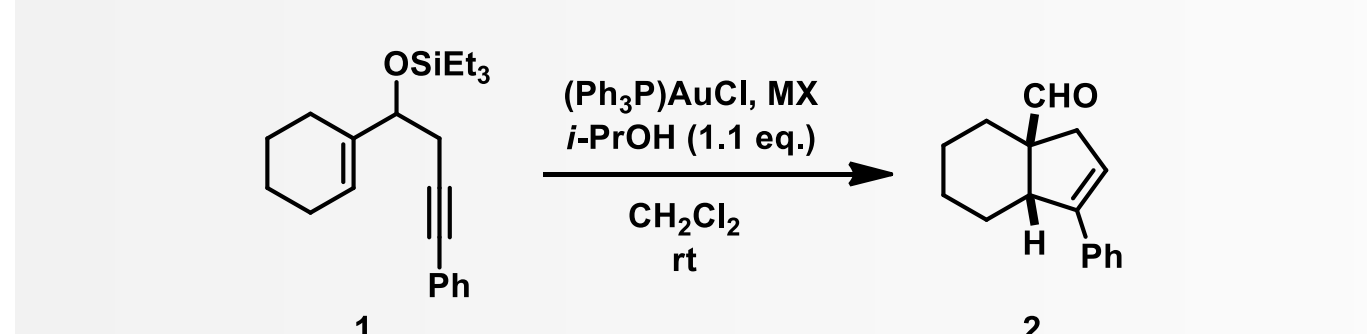
In the case of such substrates featuring a terminal alkyne moiety, the advantage of Na[Me₃NB₁₂Cl₁₁] in this reaction is mostly a practical one. However, internal alkyne **5** is a prime example for the complications associated with silver salt activation: preactivation of the catalyst with AgSbF₆ gives only traces of the product:



Entry	Catalyst (mol%)	Time [h]	3 [%] ^a	4 [%] ^a
1	AgSbF ₆ (5)	3	0	64
2	(Ph ₃ P)AuCl (5)	24	0 ^b	0
3 ^c	(Ph ₃ P)AuCl (10)/AgNTf ₂ (5)	6	65	0
4 ^{c,d}	(Ph ₃ P)AuCl (10)/AgOTf (5)	22	60	0
5 ^c	(Ph ₃ P)AuCl (10)/AgSbF ₆ (5)	1	73	0
6 ^c	(Ph ₃ P)AuCl (5)/NaBAR ^F ₄ (5)	2	59	0
7 ^c	(Ph ₃ P)AuCl (5)/Na[Me ₃ NB ₁₂ Cl ₁₁] (5)	2	73	0
8	Na[Me ₃ NB ₁₂ Cl ₁₁] (5)	24	0 ^b	0

^a Isolated yield after column chromatography. ^b No reaction. ^c (Ph₃P)AuCl and silver salt were stirred separately and filtered through Celite before addition to substrate. ^d Reaction was performed at rt. ^e (Ph₃P)AuCl and MX were directly added to substrate.

Application of Na[Me₃NB₁₂Cl₁₁] in literature-known reactions

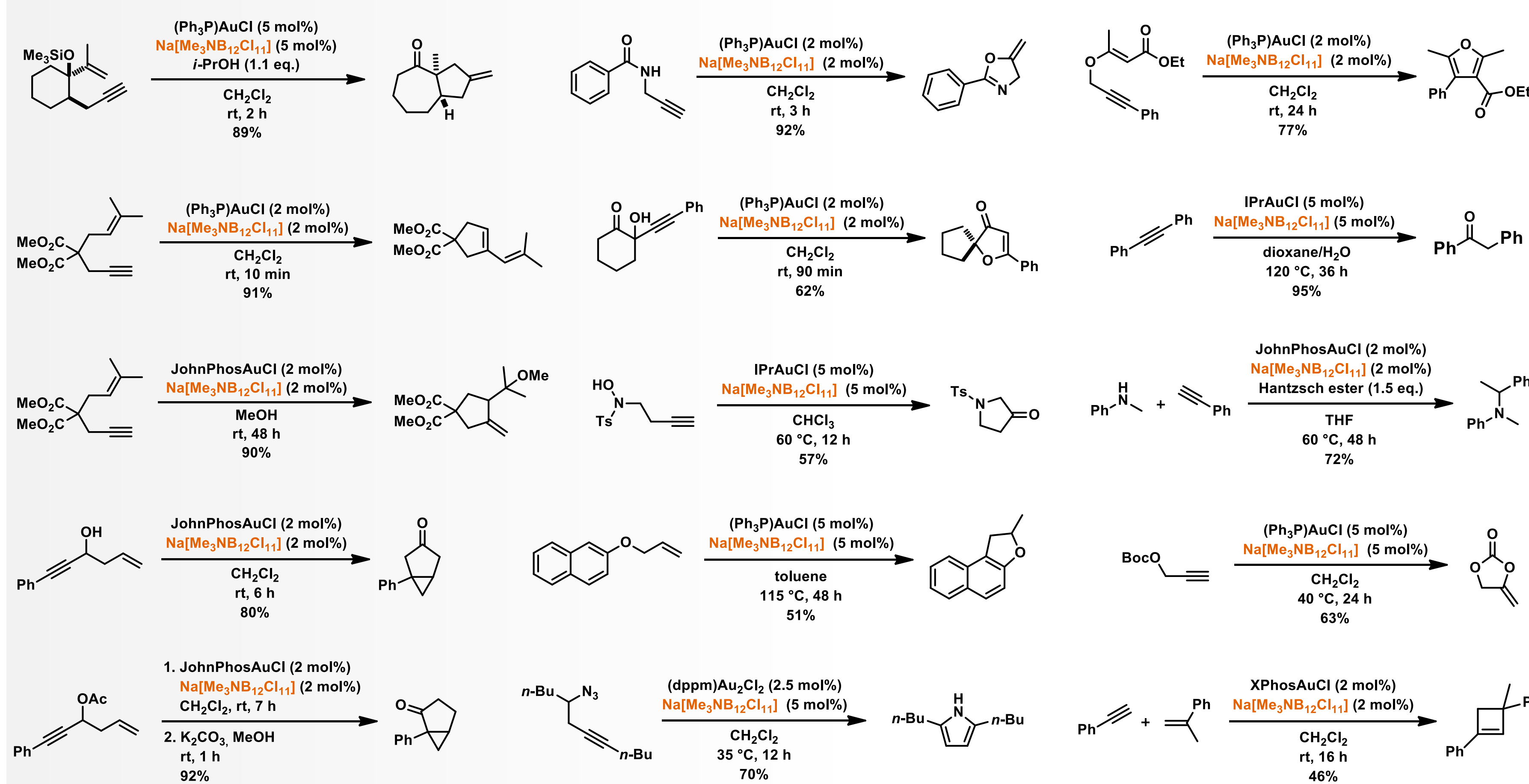


Entry	MX	Time [h]	2 [%] ^a	1 [%] ^a
1 ^b	Na ₂ [B ₁₂ H ₁₂]	24	11	71
2 ^b	Na ₂ [B ₁₂ F ₁₂]	24	0	100
3 ^b	Na ₂ [B ₁₂ Cl ₁₂]	3	66	-
4 ^b	Na ₂ [B ₁₂ Br ₁₂]	24	50	31
5 ^b	Na ₂ [B ₁₂ I ₁₂]	24	28	39
6 ^b	Li ₂ [B ₁₂ Cl ₁₂]	48	43	37
7 ^b	K ₂ [B ₁₂ Cl ₁₂]	48	37	48
8 ^b	Cs ₂ [B ₁₂ Cl ₁₂]	24	0	100
9 ^c	Na[Me ₃ NB ₁₂ Cl ₁₁]	1	92	-

^a Isolated yield after column chromatography. (Ph₃P)AuCl and MX were directly added to substrate. ^b 10 mol% (Ph₃P)AuCl, 5 mol% MX. ^c 5 mol% (Ph₃P)AuCl, 5 mol% Na[Me₃NB₁₂Cl₁₁].

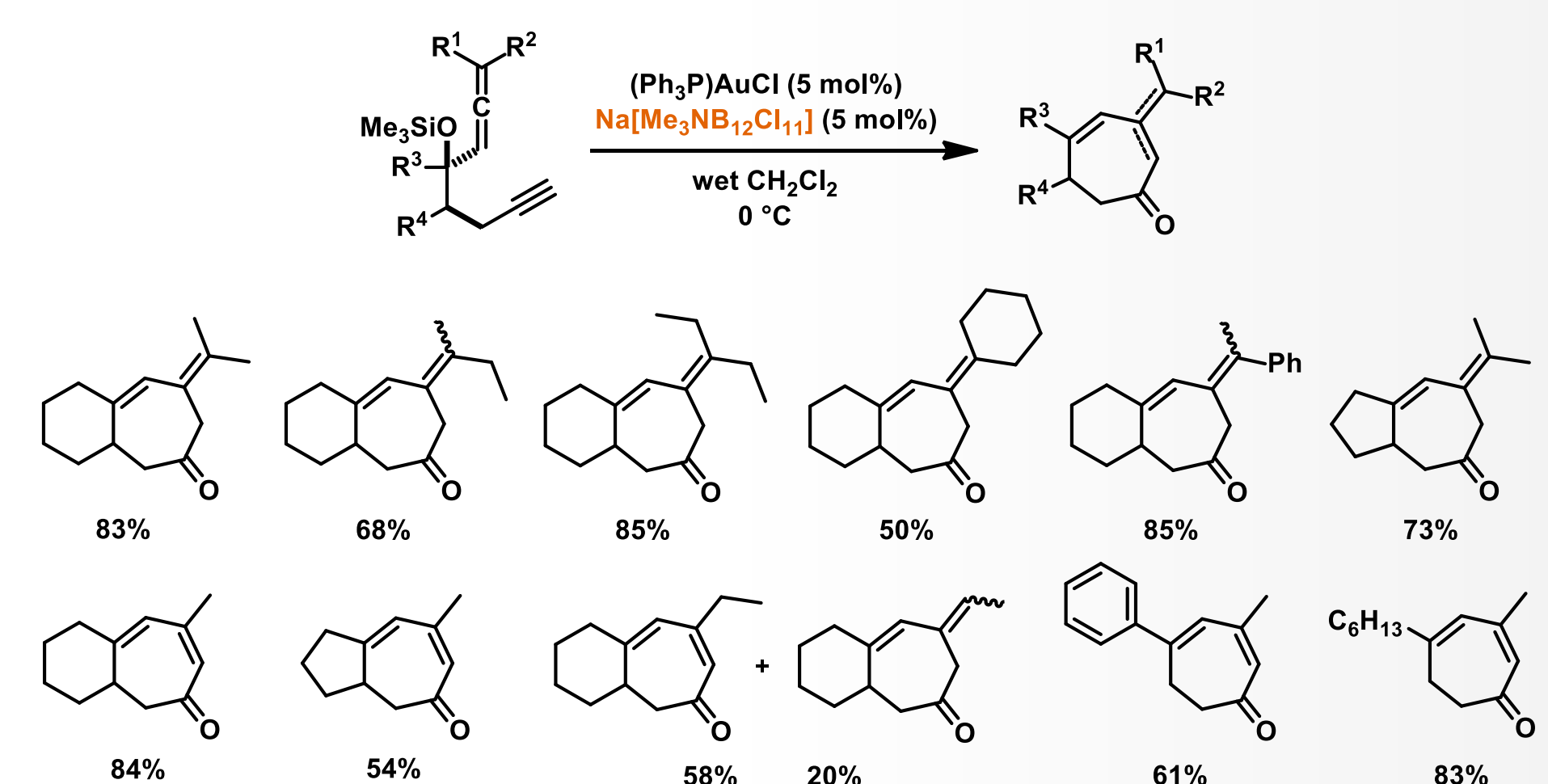
In an effort to find alternative, silver-free reagents for the activation of gold(I) chlorides, investigations of icosahedral borates as weakly coordinating anions inspired us to test a variety of such clusters (in the form of their alkali metal salts) as reagents for the *in situ* generation of catalytically active gold(I) species. In the cascade reaction of enyne **1**, the recently developed Na[Me₃NB₁₂Cl₁₁]^[4] emerged as the most promising reagent.

It was next applied to a broad spectrum of known, gold(I)-catalyzed transformations in order to test its general applicability. In these experiments, the gold(I) precatalyst was usually activated in the presence of the substrate, without any intermediary purification step. The use of Na[Me₃NB₁₂Cl₁₁] in a variety of carbocyclization, heterocyclization and other reactions (with different complexes and under a wide range of conditions) resulted in mostly excellent to moderate yields.

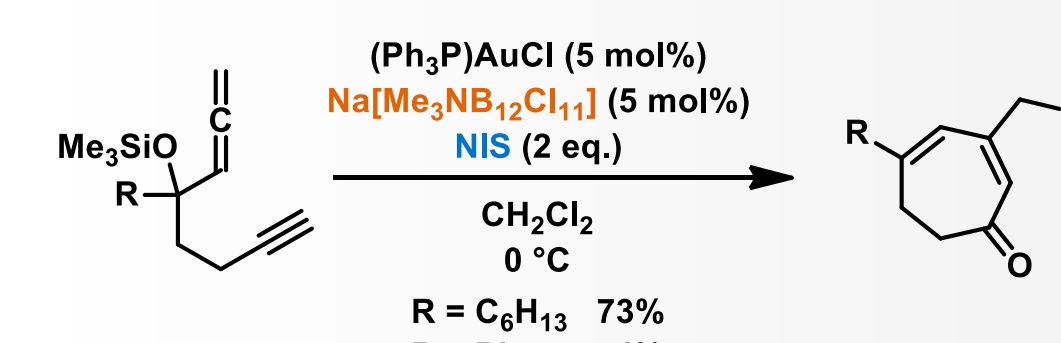


Scope of the reaction

The reaction tolerates a variety of substituents on the allene moiety and works well with both cyclic (5- and 6-membered rings) and acyclic substrates. Depending on the nature of the allene, the product features either an *exo*-cyclic double bond or an α,β-unsaturated ketone.

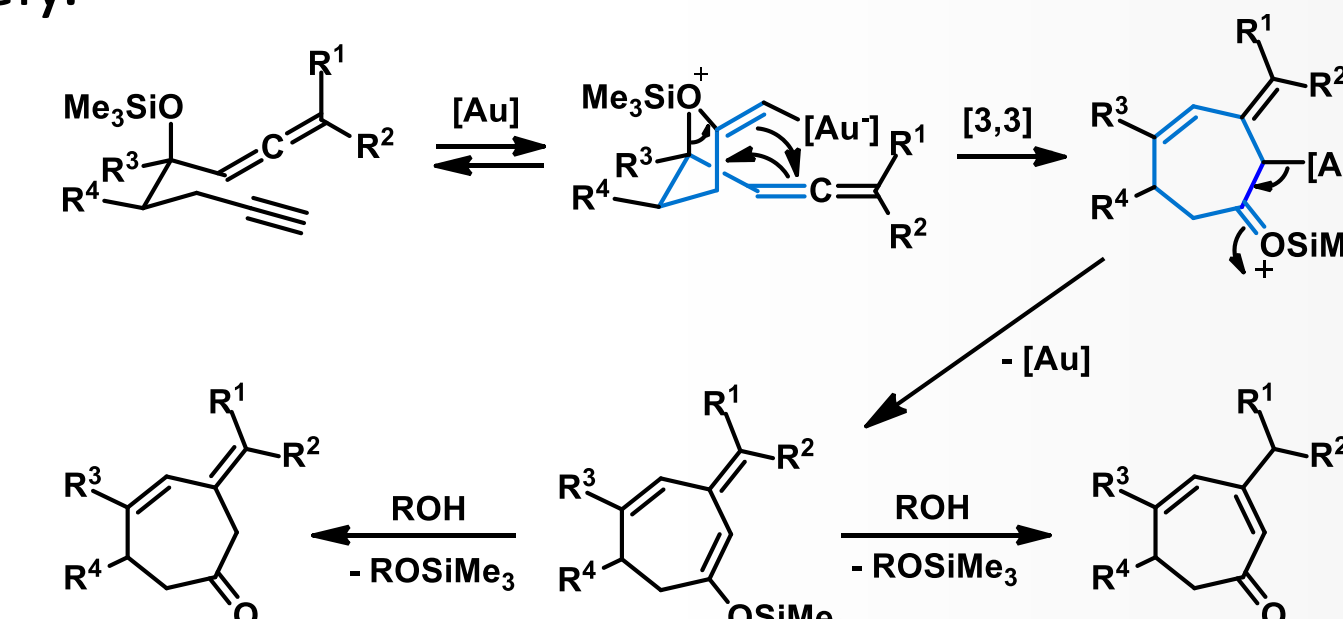


Performing the same reaction in the presence of NIS, unusual allylic iodides are formed.



Proposed mechanism

The reaction is likely to proceed via activation of the alkyne by the gold catalyst towards heterocyclization, which is followed by a [3,3] sigmatropic rearrangement and release of the catalyst. The intermediately formed silyl enol ether is then hydrolyzed to the ketone, in which case protonation can occur at either α- or γ-positions, leading to the *exo*- or *endo*-cyclic double bond, respectively.



Alternative, silver-free methods for the activation of gold(I) catalysts are of increasing interest. We report the successful application of Na[Me₃NB₁₂Cl₁₁] as a facile means for the *in situ* activation of gold(I) chloride complexes. The reactivity of the resulting active species is demonstrated with a broad variety of known reactions as well as an unprecedented cascade reaction of 5-siloxy-1,6-allenynes.



[1] M. Wegener, F. Huber, C. Bolli, C. Jenne, S. F. Kirsch, *submitted for publication*. [2] D. Wang, R. Cai, S. Sharma, J. Jirak, S. K. Thummanapelli, N. G. Akhmedov, H. Zhang, X. Liu, J. L. Petersen, X. Shi, *J. Am. Chem. Soc.* **2012**, *134*, 9012. [3] A. Homs, I. Escofet, A. M. Echavarren, *Org. Lett.* **2013**, *15*, 5782. [4] C. Bolli, J. Derendorf, C. Jenne, H. Scherer, C. P. Sindlinger, B. Wegener, *Chem. Eur. J.* **2014**, *accepted manuscript*.

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