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Ligand-Controlled Access to [4+2] and [4+3]-Cycloadditions in Gold-Catalyzed Reactions of Allene-Dienes

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Abstract

By adjusting the electronic properties of the ancillary ligands high selectivity can be achieved for either gold(I)-catalyzed [4+2]- or [4+3]-cycloaddition reactions of diene-allenes.

Triarylphosphitegold(I) complexes are employed as catalysts for a [4+2]-cycloaddition reactions leading to alkylidenecyclohexenes. Conversely, di-*t*-butylbiphenylphosphinegold(I)-catalyzed reactions afford cycloheptadienes via [4+3]-cycloaddition reactions.

The utility of homogenous transition metal catalysis derives, in part, from the ability to influence the outcome of the catalyzed reaction by variation of the ancillary ligands.¹ We were initially attracted to LAu(I)X complexes as catalysts due to the potential of controlling reactivity² and stereoselectivity³ by manipulating the neutral(L) and/or anionic(X)⁴ ligands. While these ligand effects on catalysis with cationic gold(I) complexes have been demonstrated, examples of ligand variation as a means to achieve divergent reactivity in gold-catalyzed reactions remain elusive.^{5,6} In this context, we were intrigued by the observation that, in sharp contrast to the selective [2+2]-cycloaddition of allenes,⁷ the triphenylphosphinegold(I)-catalyzed reaction of allene-diene **1** provided a 2:1 mixture of the [4+3]⁸ and [4+2]⁹ cycloadducts (eq 1). We were, therefore, attracted to the possibility that either cycloadduct could be accessed by variation of the ligand on the gold(I) catalyst.

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Supporting Information Available: Experimental procedures and compound characterization data (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

(1)

We hypothesized that the product selectivity in gold(I)-catalyzed cycloaddition reactions could be impacted by modulating the relative stability of the cationic transition states generated during the course of the cycloadditions. In particular fine tuning of the electronic properties of the catalyst should have a direct impact on the stability of gold(I)-carbenoid intermediate **A** formed in the [4+3]-cycloaddition.¹⁰ For example, we posited that the pathway leading to the [4+3]-cycloadduct could be favored by employing electron-rich σ -donor ligands that would increase the relative stability of pathway leading to **A**, while having significantly less impact on the formation of **B**.

In accord with this hypothesis, replacing Ph_3P with the Takasago BRIDP ligands¹¹ resulted in highly selective formation of the seven-membered ring (Table 1, entries 2-5). Unfortunately, these reactions, as well as that catalyzed by $(\text{IPr})\text{gold}(\text{I})$, produced varying amounts of olefin isomerization to cycloheptadiene isomer **3'**. The selectivity was improved to 96:4 in favor of the [4+3]-cycloadduct **3** using di-*t*-butylbiphenylphosphinegold(I)¹² as the catalyst (entry 6). Encouraged by these results, we considered that π -acceptor ligands might decrease the relative stability of **A** and therefore divert the reaction to the [4+2]-cycloadduct. Gratifyingly, the use of arylphosphitegold(I)^{5b,13} complexes produced exclusively the formal [4+2]-cycloaddition product **2** in very good yields after 30 minutes (entries 8 and 9).

With these results in hand, we examined the scope of the gold(I)-catalyzed cycloaddition reactions. The triarylphosphitegold(I)-catalyzed [4+2] cycloaddition showed excellent tolerance for substitution on the diene component (examples **2**, **4-6** in Scheme 1). For example, a 1,1-disubstituted diene underwent the gold-catalyzed [4+2]-cycloaddition to afford cycloadduct **5** containing a quaternary carbon. Variations in the tether were also accepted, as demonstrated by the cycloaddition leading to pyrrolidine **8**. In all cases the reactions were highly diastereoselective, affording exclusively the *trans*-fused cycloadduct.^{14,15} With the exception of the formation of **4**, the arylphosphitegold(I)-catalyzed reaction was highly selective for the [4+2]-cycloadduct.

The phosphinegold(I)-catalyzed [4+3]-cycloaddition also showed excellent scope. The reaction also tolerated variation in the tether, allene and the alkene substituents (Scheme 2). For example, a *trans,trans*-1,4-disubstituted diene underwent the gold-catalyzed cycloaddition to afford cycloheptadiene **13** as a single diastereomer. Moreover, in accord with our previous observations,¹⁶ treatment of **1** with 5 mol % $\text{IPrAuCl}/\text{AgSbF}_6$ in the presence of excess diphenylsulfoxide led to formation of *trans*-fused bicyclic ketone **14** in 53% yield (eq 2).

(2)

In contrast to the stereochemical outcome of the related [2+2]-cycloaddition reaction,⁷ gold (I)-catalyzed [4+2] and [4+3]-cycloaddition reactions of deuterium-labeled dienes **15** and **16** were stereospecific (eq 3). For example, di-*t*-butylbiphenylphosphine-gold(I)-catalyzed reaction of **15** gave **17** as a single diastereomer (for additional details see supporting information). This observation suggests that the [4+2] and [4+3]-cycloaddition reactions may proceed through concerted mechanisms;⁸ however, a step-wise mechanism involving generation of an allyl cation from the addition of the diene to a gold-activated allene can not be excluded.^{15,17}

(3)

On the basis of these results, we revisited the reaction gold(I)-catalyzed of allenenes to determine whether ligand-control could be employed to divert the previously reported [2+2]-cycloaddition reaction⁷ towards the [3+2]-cycloaddition reaction manifold. We were pleased to find that the di-*t*-butylbiphenylphosphinegold(I)-catalyzed reaction of phenyl-substituted enallenenes led to exclusive formation of cyclopentene cycloadducts **21** and **22** as single diastereomers in high yield (eq 4). In this case, the reaction likely proceeds *via* a step-wise mechanism,¹⁸ in which ligand effects stabilize the pathway proceeding through gold(I)-stabilized cation **C**.

(4)

In conclusion, we have demonstrated that high selectivity can be achieved for gold(I)-catalyzed intramolecular [4+2]- and [4+3]-cycloaddition reactions of diene-allenes. The studies presented herein lend further support to the hypothesis that the gold(I) complexes are capable of stabilizing adjacent carbocations, such as **A** and **C**, and that this stabilization can be modulated by adjusting the electronic properties of the ancillary ligands. Given that this class of intermediate is prevalent in gold(I)-catalyzed transformations,¹⁹ the development of reactions that take advantage of this ligand-controlled reactivity is ongoing and will be reported in due course.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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^a Isolated as a 81:19 mixture of **4**:**10**

Scheme 1.
[4+2]-Cycloaddition of Allene-dienes

Scheme 2.
[4+3]-Cycloaddition of Allene-dienes

Table 1
Ligand effects on product distribution^a

entry	Ligand (L)	2 : 3 : 3' ^b	% yield ^b
1	Ph ₃ P	67:33:0	80
2	cy-cBRIDP	22:58:20	66
3	cy-vBRIDP	17:67:16	73
4	cBRIDP	17:73:10	74
5	vBRIDP	7:87:6	80
6	IPr	7:89:4	75
7	di- <i>t</i> -butylbiphenylphosphine	4:96:0	89
8	Tris(2,4-di- <i>t</i> -butyl phenyl)phosphite	100:0:0	91
9	(PhO) ₃ P	100:0:0	89

^aReaction conditions: 0.1 M allene-diene in CH₂Cl₂, 5 mol% LAuCl, 5 mol% AgSbF₆, rt.

^bDetermined by ¹H NMR using 1,3,5-trinitrobenzene as internal standard.