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Monomeric Linear Diaminocarbene Complexes of Gold(I) Show Merit in Enantioselective Catalysis

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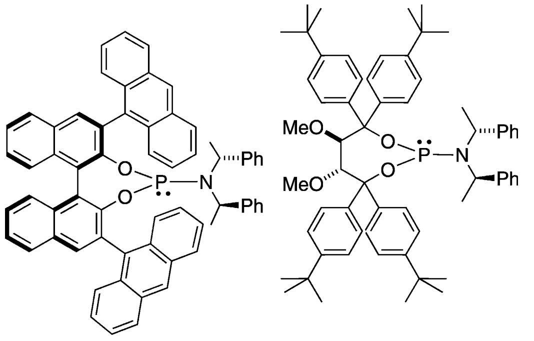
In the extremely active field of homogeneous gold catalysis, various ancillary ligand types such as phosphines, phosphites, and some N-heterocyclic carbenes[1] have been recently coordinated to gold(I) to form active catalysts for organic transformations. Acyclic diaminocarbenes (ADCs), also known as nitrogen acyclic carbenes (NACs), now deserve to also be mentioned here, although the full scope of their tailorability and appositeness still has to be determined.

Since 2008, the groups of Echavarren, Espinet, Hashmi, Merz, Hong, and others have been actively engaged in studying the structures, catalytic activity, and chemoselectivity of ADC complexes using a wide variety of unsaturated substrates.[1a–f] Echavarren, Espinet, and co-workers[2] introduced complexes of the generally less-active hydrogen-bond-supported heterocyclic carbenes (HBHCs), within the same family of ligands. Very recently, Handa and Slaughter[3] accomplished the first highly successful enantioselective transformations using linear chiral ADC complexes of gold as precatalysts.

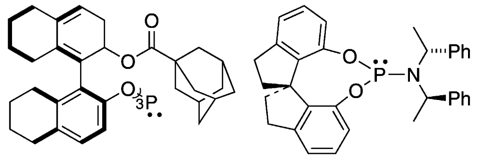
Of the significant number of successful enantioselective reactions with gold complexes known,[4] most involve dinuclear gold complexes. To date, carbene complexes have mostly been mediocre or, at best, moderately successful catalysts (although excellent selectivities have recently been reported with dinuclear gold carbene complexes; see below[5]). Various investigations, mainly with cycloadditions of allenenes and allenedienes, carried out in particular by the groups of Mascareñas,[6] Fürstner,[7] and Toste,[8] using only a few chiral phosphoramidite or phosphite complexes (see Scheme 1 for examples of ligands; others are given in the Supporting Information), have been extremely successful and also highlight the difficulties involved in enantioselective catalysis with the monomeric gold complexes $[LAu]^+$.[9]

The phosphoramidite **1** (Scheme 1) required bulky substituents, whereas **2** was suitably fitted with electron-rich aromatic substituents for π interaction with the metal. Notably, the requirements for enantioselectivity of the catalyst are superimposed on those for kinetic and stereochemical efficiency, and in certain instances the latter two features could be inversely influenced by the former.



(*R,R,R*)-**1**, Ref. [6]

(*R,R,R*)-**2**, Ref. [7]



(*S*)-**3**, Ref. [8a]

(*R,R,R*)-**4**, Ref. [8b]

Scheme 1. Representative examples of ligands with binol [(*R,R,R*)-**1**], taddol [(*R,R,R*)-**2**], and H8-binol [(*S*)-**3**] chiral backbones. The ligand (*R,R,R*)-**4** is a Siphos-derived diastereomer.

Recent investigations by others have also provided important preliminaries to the work of Handa and Slaughter described below while the same group previously described the first chiral ADC-derived complex (of Pd^{II}).[10] Exo-bidentate ADC ligands that contain phenyl substituents in the 3,3′-positions of a binol backbone (see the Supporting Information) were prepared by Espinet and co-workers.[11] The dinuclear gold complexes made therefrom are only moderately enantioselective catalysts. The ligands were further modified by Toste and co-workers[5] by affixing larger 4-substituted aryl units in the 3,3′-positions and changing the chirality. The selected anionic counterions and reaction temperature are important additional selectivity variables. Their propargyl ester reactions occur with high enantioselectivities, but neither the influence of the substituted aromatic groups attached to the chiral naphthyl nor the role played by

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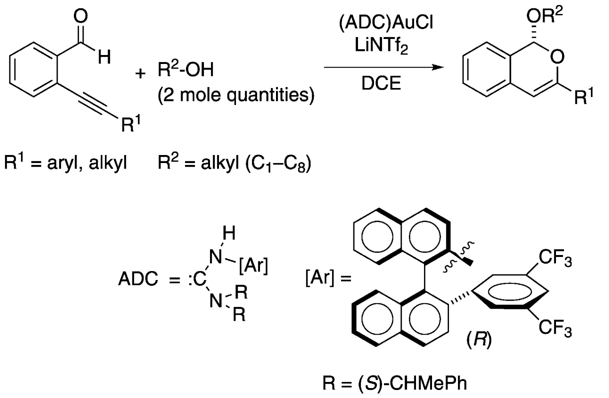
the second gold center in the catalyst has been clarified conclusively.

Handa and Slaughter then chose to use ADC gold complexes, [(ADC)AuCl]—prepared according to the classical isocyanide route[12]—in the presence of dechlorinating LiNTf$_2$ to catalyze a tandem acetylization/cycloisomerization reaction [Eq. (1); DCE = 1,2-dichloroethane, Tf = trifluoromethanesulfonyl]. Satisfactory yields were obtained albeit at a moderate reaction rate, even at 25 °C. The particular relevance of the results obtained lies in the rather simple manner in which the chiral information is made available to the active metal center and in the superb enantioselectivity realized. For the most successful precatalyst, the ADC ligand bears three chiral substituents with a (*R*,*S*,*S*) matched conformation.



(1)

To enhance chirality transfer by the rather remotely positioned chiral ligand in linear, monomeric gold(I) complexes, the chiral pocket around the metal has to be tightened. In contrast to previous examples of such complexes having strong π-accepting ligands, where bulky substituents and through-space Au–π electrostatic interactions have been employed, Handa and Slaughter attached electron-poor $C_6H_3(CF_3)_2$ substituents to the binol-derived binaphthalide. The resulting interaction with the metal is most likely modulated by the strong σ-donating ADC ligand which renders the metal less positively charged. Crystal structure determination clearly indicates that the $C_6H_3(CF_3)_2$ groups are positioned in close proximity (ca. 3.5 Å) to the metal, whereas corresponding, unsubstituted C_6H_5 groups show no affinity for the active center. The results obtained seem to suggest that the effective mimicking of disproportional bidentate coordination in a push-pull fashion is maintained in solution. Depending upon the substituents R^1 and R^2 on the substrates, enantiomeric excesses of between 89 and greater than 99 % have been realized. Only for cases where both R^1 and R^2 are alkyl (specifically $R^2 = Me$) has the enantioselectivity been unsatisfactory (ca. 60 % *ee*). One could, in accordance with calculations made by the group of Toste,[8b] hypothesize that the major contribution to the enantioinductive ligands is made by the binaphthyl backbone on the one N atom and ably leveraged by the chirality in the (*S*,*S*)-bis(phenylmethyl)amine unit positioned at a completely different angle to the gold atom, but more evidence is required before this dynamic system is fully understood.

The outstanding communication by Handa and Slaughter opens up many new avenues for future investigation. The mechanism of their chosen reaction is not yet known, although a tentative working hypothesis has been proposed for a related reaction by Belmont and co-workers.[13] Exactly how the hemiacetalization by R^2OH is catalyzed and at what stage it occurs is not yet clear. The availability of new σ-donating ADC enantioinductive ligands, or variations thereof, could be an impetus for their evaluation in many other reactions, such as cyclizations of 1,6-allenedienes and allenenes, where inverse induced regioselectivity compared to that of the chiral π-acceptor phosphoramidites is to be expected.

Existing synthetic approaches for the preparation of ADC complexes[14] could be modified and then exploited for the synthesis of chiral gold complexes. Expansion into the field of other chiral acyclic carbenes,[15] even of the more typical Fischer or even Schrock types, presents challenges and opportunities for synthetic chemists. The flexible acyclic catalytic system, and particularly the advantage that the relatively large X-C_{carb}-Y angle offers, can be maintained, while the electron-donating properties and mode of effective chirality transfer are varied.

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