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Cyclometallated Gold(III) Complexes as Effective Catalysts for Synthesis of Propargylic Amines, Chiral Allenes and Isoxazoles

Karen Ka-Yan Kung,[a] Vanessa Kar-Yan Lo,[b] Hok-Ming Ko,[a] Gai-Li Li,[a] Pui-Ying Chan,[a] King-Chi Leung,[a] Zhongyuan Zhou,[a] Ming-Zhong Wang,[b] Chi-Ming Che,[b,*] and Man-Kin Wong[a,*]

[a] State Key Laboratory of Chirosciences and Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hung Hom, Hong Kong, People's Republic of China
Fax: (+852)-2364-9932; e-mail: mankin.wong@polyu.edu.hk

[b] State Key Laboratory of Synthetic Chemistry, Department of Chemistry and Open Laboratory of Chemical Biology of the Institute of Molecular Technology for Drug Discovery and Synthesis, The University of Hong Kong, Pokfulam Road, Hong Kong, People's Republic of China
Fax: (+852)-2857-1586; e-mail: cmche@hku.hk

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Abstract: A series of cyclometallated gold(III) complexes $[Au(\widehat{CN})Cl_2]$ **1a–l** ($H\widehat{CN}$ = arylpyridines) and a PEG-linked complex **1m** were synthesized. Complexes **1a–m** are effective in catalyzing the synthesis of propargylic amines, chiral allenes and isoxazoles. Six-membered ring cyclometallated gold(III) complexes **1f–l** exhibited higher catalytic activity than five-membered ring cyclometallated gold(III) complexes **1a–e**. The diastereoselectivity of propargylic amines could be tuned by using chiral aldehyde and/or amine substrates. Excellent enantioselectivities (90–98% *ee*) were achieved in chiral allene synthesis. Chiral allene racemization could be minimized by using **1f** as catalyst. The PEG-linked catalyst **1m** is the most catalytically active towards synthesis of propargylic amines, in which case a product turnover of 900 was achieved. Moreover, **1m** could be repeatedly used for 12 reaction cycles, leading to an overall turnover number of 872.

Keywords: allenes; cyclometallation; gold catalysis; isoxazoles; propargylic amines

Introduction

Gold catalysis has exerted a significant impact on organic chemistry in the past decade.[1] Owing to their carbophilic characters, gold complexes are highly efficient in catalyzing the activation of C/C multiple bonds,[2] such as alkenes, alkynes and allenes, towards nucleophilic attacks, leading to the formation of C–C, C–N, C–O, and C–S bonds and in the activation of C–H bonds[3] of terminal alkynes and arenes, generating organogold intermediates for C–C bond forming reactions. The unique advantages of gold catalysts including excellent reactivity and selectivity, high functional group tolerance, and exceptional insensitivity to air and aqueous reaction conditions are highly desirable for organic synthesis and for the development of sustainable catalysis.[4]

Significant advances in the development of gold(I) catalysts have been made. Through judicious ligand design, gold(I) phosphine and N-heterocyclic carbene (NHC) complexes have been found to exhibit superior catalytic activity and selectivity over simple gold(I) salts.[5] Chiral gold(I) phosphine and NHC complexes are also excellent catalysts for asymmetric synthesis.[6]

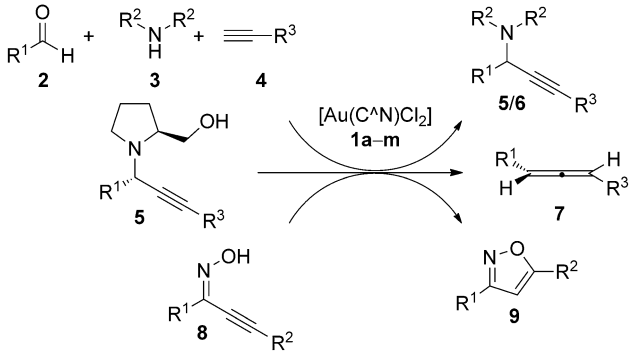
Gold(I) catalysts are usually two coordinated with a linear geometry. Thus the chiral auxiliary ligand(s) is distant from the substrates, consequently special attention in the molecular design of chiral environment in Au(I) catalyst is required. In contrast, gold(III) catalysts have a planar coordination geometry, and hence the spatial environment around the gold(III) reaction center can be more easily fine-tuned through ligand design studies, leading to different classes of coordination[7] and organometallic[8] gold(III) compounds. Promising catalytic activities have been reported using gold(III) complexes as catalysts.[9a]

Cyclometallated gold(III) complexes containing bidentate C,N ligands have been investigated for their biological activities and for the development of new luminescent materials.[9b] However, the use of cyclo-

metallated gold(III) complexes as catalysts in organic synthesis is largely unexplored.[10]

Over the years, we have been developing gold catalysis for organic transformation reactions.[11] In 2009, we reported that cyclometallated gold(III) complex $[Au(ppy)Cl_2]$ **1a** (Hppy = 2-phenylpyridine) was an effective catalyst for diastereoselective synthesis of propargylic amines *via* a three-component coupling reaction of aldehydes, amines and alkynes in excellent yields (up to 98%) and diastereoselectivities (up to 99:1) by using chiral amines.[11f] Notably, the cyclometallated gold(III) catalyst could be repeatedly used for three cycles with 252 product turnovers and ten cycles with 812 product turnovers without significant loss of catalytic activity. Recently, we applied this cyclometallated gold(III) complex-catalyzed reaction for bifunctional modification of aldehyde-containing oligosaccharides in excellent substrate conversions (up to 99%) with high functional group tolerance in an aqueous medium under mild reaction conditions.[11k]

Herein we report the design and synthesis of a series of cyclometallated gold(III) complexes $[Au(\widehat{CN})Cl_2]$ **1a–m** ($H\widehat{CN}$ = arylpyridines) and investigations of their catalytic activities in catalyzing three mechanistically diverse organic transformation reactions including synthesis of propargylic amines (**5**/**6**), chiral allenes (**7**), and isoxazoles (**9**). It is envisioned that studies on the catalytic activities of structurally well-defined gold(III) catalysts would provide knowledge for the future development of gold(III) catalysis (Scheme 1).



Scheme 1. Cyclometallated gold(III) complex-catalyzed organic transformation reactions.

Results and Discussion

Preparation of Cyclometallated Gold(III) Complexes 1a–l

Cyclometallated gold(III) complexes **1a**,[12] **1b**,[13] **1e**,[14] **1f**, **1g**,[15] **1i**[16] and **1k**[17] were synthesized and characterized according to literature reports. New complexes **1c** and **1d** were prepared by transmetallation reaction, while **1h** and **1j** were prepared by direct cycloauration reactions (Figure 1). The molecular structure of **1j** was confirmed by X-ray crystallography (Scheme S1, Supporting Information). Complex **1k** was synthesized by a modified procedure of silver-ion assisted cycloauration reaction using a simple silver salt, $AgNO_3$, that could be used in place of the expensive silver salt, AgO_2CCF_3.

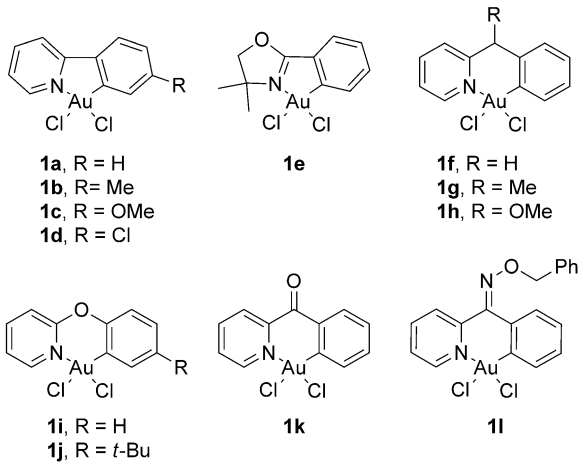


Figure 1. Cyclometallated gold(III) complexes used in catalyzing organic transformation reactions.

We employed the ketone moiety of **1k** for further synthetic elaboration. By reaction of **1k** with *O*-benzylhydroxylamine hydrochloride under the conditions of aniline-catalyzed oxime formation,[18] an oxime-containing cyclometallated gold(III) complex **1l** was obtained. We envisioned that **1k** could act as a building block for the synthesis of soluble polymer-supported catalysts (see below). All of the gold(III) complexes were characterized by ^1H NMR, ^{13}C NMR, and ESI-MS, and were found to be air- and water-stable.

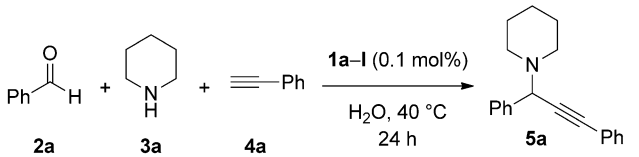
Cyclometallated Gold(III) Complexes for Three-Component Coupling Reaction of Aldehydes, Amines and Alkynes

Propargylic amines are key building blocks commonly encountered in synthetic chemistry, bioorganic chemistry, and natural product synthesis.[19] Propargylic amine synthesis through transition metal-catalyzed three-component coupling reaction is an efficient approach owing to its high efficiency and excellent atom-economy.[20,21] Particularly, gold catalysts such as $AuBr_3$,[21a] Au/CeO_2 and Au/ZrO_2[21b] were found to be effective for this reaction, but high reaction temperatures (i.e., 100 °C) and/or reactions under nitrogen were required. Although $[Au(Salen)PF_6]$ is catalytically active at lower reaction temperatures, giving

a product turnover number (TON) of 820 with 0.05 mol% loading at 40 °C,[11a] the reactions still need to be conducted under nitrogen.

In our previous studies, we demonstrated that cyclometallated gold(III) complexes **1a** and **1f** could catalyze the reactions under nitrogen[11f] and air,[11k] respectively. In the present work, the catalytic activities of gold(III) complexes **1a–l** were examined by stirring the corresponding catalyst (2 μmol, 0.1 mol%), benzaldehyde **2a** (2 mmol), piperidine **3a** (2.2 mmol) and phenylacetylene **4a** (3 mmol) in water (1 mL) at 40 °C for 24 h under air. On the basis of ^{1}H NMR analysis of the crude reaction mixture, substrate conversion and the corresponding isolated yield were obtained and used to determine the TON. For catalysts **1a–e** with five-membered rings, TON of 260-490 were obtained (Table 1, entries 1–5). Six-membered ring cycloaurated complexes **1f–l** gave TON of 370–770 (entries 6–12). Our results revealed that the C,N ligands in cyclometallated gold(III) complexes **1a–l** could help to enhance their catalytic activities during the reactions. In this regard, **1f** was chosen for further studies in the synthesis of optically active propargylic amines, as its ligand (HCN = 2-benzylpyridine) is commercially available and inexpensive.

Table 1. Screening of various cyclometallated gold(III) complexes for propargylic amine synthesis *via* a three-component coupling reaction of benzaldehyde **2a**, piperidine **3a**, and phenylacetylene **4a**.[a]



2a **3a** **4a** **5a**

Entry	Catalyst	Conversion [%][b]	Yield [%][c]	TON[d]
1	**1a**	33	86	280
2	**1b**	32	80	260
3	**1c**	36	90	320
4	**1d**	56	87	490
5	**1e**	59	61	360
6	**1f**	82	83	680
7	**1g**	72	75	540
8	**1h**	63	62	390
9	**1i**	62	66	410
10	**1j**	50	74	370
11	**1k**	81	93	750
12	**1l**	91	85	770

[a] *Reaction conditions:* catalyst **1a–l** (2 μmol), benzaldehyde **2a** (2 mmol), piperidine **3a** (2.2 mmol) and phenylacetylene **4a** (3 mmol) in water (1 mL).
[b] Determined by ^{1}H NMR analysis of crude reaction mixture based on benzaldehyde conversion.
[c] Isolated yield based on benzaldehyde conversion.
[d] TON = turnover numbers, which were calculated from isolated yield of product based on benzaldehyde conversion.

Use of Chiral Amines for Diastereoselective Synthesis of Propargylic Amines

The effect of chiral amines on diastereoselectivity was studied in the three-component coupling reaction with **1f** as catalyst. Using prolinol **3b** and prolinol methyl ether **3c** as the amine components, the coupling products **5b** and **5c** were obtained in 68% and 70% yields, respectively, with a diastereomeric ratio (*dr*) of 95:5 (Table 2, entries 1 and 2). Comparable yields (68% and 80%) and *dr* values of 95:5 for propargylic amines **5d** and **5e** that bear opposite chirality to **5b** and **5c** were found (entries 3 and 4). Excellent diastereoselectivity (>99:1) of propargylic amine **5f** was observed for the coupling reaction of a prolinol that has a bulky diphenyl group (entry 5).

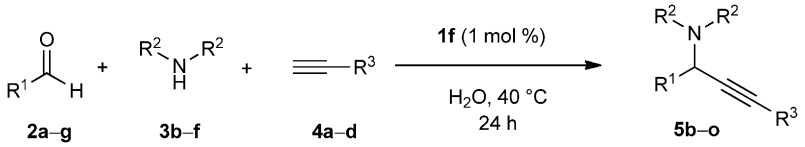
The **1f**-catalyzed three-component coupling reaction also worked well for other alkyne substrates. Coupling of L-prolinol **3b** and arylacetylenes bearing electron-donating (*p*-MeO) and electron-withdrawing (*p*-Cl) groups led to propargylic amines **5g** and **5h** in 70% yields with *dr* values of 92:8 and 96:4, respectively (entries 6 and 7). Changing the alkyne component to 1-ethynylcyclohexene **4d** gave **5i** in 95:5 diastereoselectivity (entry 8).

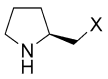
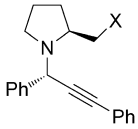
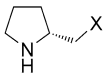
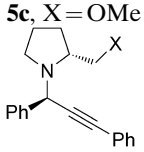
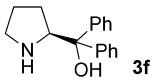
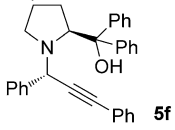
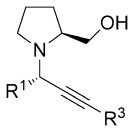
Varying the substitution on aldehyde components afforded propargylic amines **5j–n** in good to excellent yields (63–97%) and with excellent *dr* values of up to 95:5 (entries 9–13). Interestingly, coupling of isovalerylaldehyde **2g** with prolinol **3b** and phenylacetylene **4a** gave propargylic amine **5o** with an excellent *dr* value of >99:1 (entry 14), and the latter was characterized by X-ray crystallography for resolving the absolute configuration (Figure 2). These experiments revealed that the diastereoselectivity of the newly formed sp^3 carbon center of the propargylic amine could be controlled by the chirality of the prolinol. In addition, the methyl ether and hydroxy groups remained intact after the coupling reactions.

Selective Modification of Aldehyde-Containing 1,2:3,4-Di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-l,5-pyranose for Synthesis of Propargylic Amine-Modified Sugars

Reports on gold-catalyzed methods for the construction of oligosaccharides and glycoconjugates are rare in the literature.[22] Recently, we have developed a cyclometallated gold(III)-catalyzed three-component coupling reaction for bifunctional modification of oligosaccharide compounds under mild reaction conditions without protection of sensitive functional

Table 2. 1f-catalyzed propargylic amine synthesis *via* a three-component coupling reaction of aldehydes **2a–g**, amines **3b–f** and alkynes **4a–d**.[a]



Entry	Aldehyde	Amine	Alkyne	Product[b]	Isolated yield [%]	*dr*[c]
						
1	**2a**	**3b**, X = OH	**4a**	**5b**, X = OH	68	95:5
2	**2a**	**3c**, X = OMe	**4a**	**5c**, X = OMe	70	95:5
						
3	**2a**	**3d**, X = OH	**4a**	**5d**, X = OH	68	95:5
4	**2a**	**3e**, X = OMe	**4a**	**5e**, X = OMe	80	95:5
5	**2a**	 **3f**	**4a**	 **5f**	76	>99:1
						
6	**2a**	**3b**	**4b**, $R^3 = p$-$MeOC_6H_4$	**5g**, R^1 = Ph, $R^3 = p$-$MeOC_6H_4$	70	92:8
7	**2a**	**3b**	**4c**, $R^3 = p$-ClC_6H_4	**5h**, R^1 = Ph, $R^3 = p$-ClC_6H_4	70	96:4
8	**2a**	**3b**	**4d**, R^3 = cyclohexenyl	**5i**, R^1 = Ph, R^3 = cyclohexenyl	51	95:5
9	**2b**, $R^1 = p$-MeC_6H_4	**3b**	**4a**	**5j**, $R^1 = p$-MeC_6H_4, R^3 = Ph	97	95:5
10	**2c**, $R^1 = p$-EtC_6H_4	**3b**	**4a**	**5k**, $R^1 = p$-EtC_6H_4, R^3 = Ph	85	95:5
11	**2d**, $R^1 = p$-(*i*-Pr)C_6H_4	**3b**	**4a**	**5l**, $R^1 = p$-(*i*-Pr)C_6H_4, R^3 = Ph	90	95:5
12	**2e**, $R^1 = p$-ClC_6H_4	**3b**	**4a**	**5m**, $R^1 = p$-ClC_6H_4, R^3 = Ph	63	95:5
13	**2f**, $R^1 = p$-BrC_6H_4	**3b**	**4a**	**5n**, $R^1 = p$-BrC_6H_4, R^3 = Ph	72	95:5
14	**2g**, R^1 = isovaleryl	**3b**	**4a**	**5o**, R^1 = isovaleryl, R^3 = Ph	60	>99:1

[a] *Reaction conditions:* catalyst **1f** (5 μmol), aldehyde **2a–g** (0.5 mmol), amine **3b–f** (0.55 mmol), alkyne **4a–d** (0.75 mmol) in water (1 mL).
[b] The absolute configuration of the major product is shown.
[c] Determined by ^{1}H NMR analysis of crude reaction mixture.

groups.[11k] In this work, the model reaction for the bifunctional modification of oligosaccharides was the coupling reaction of methyl α-D-galactopyranose (unprotected monosaccharide), **3a** and **4a**, giving propargylic amine-modified methyl α-D-galactopyranose with a *dr* value of 1:1 (Scheme 2).

We extended the substrate scope of this gold-catalyzed diastereoselective synthesis of propargylic amine-modified sugars by coupling 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose **2h** (protected monosaccharide) with various combinations of amines and alkynes.[23,24] Using **2h**, amine **3a** or **3g** and phenylacetylene **4a**, products **6a** and **6d** were obtained in up to 76% yield (Figure 3) and in a diastereomeric ratio of 97: 3 (Table 3, entries 1 and 4). These findings indicated that protection of galactose by *O*-isopropylidene groups has a significant effect on the diastereoselectivity, in which similar observations for α-oxyaldehydes as substrates have also been reported.[21c,25] The absolute configuration of all propargylic amine-modified sugars was assigned on the basis of X-ray crystallographic analysis (Figure S2,

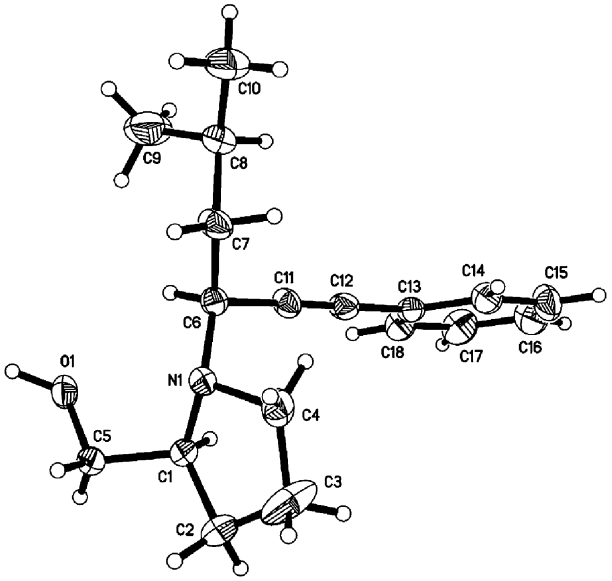


Figure 2. X-ray crystal structure of **5o**.

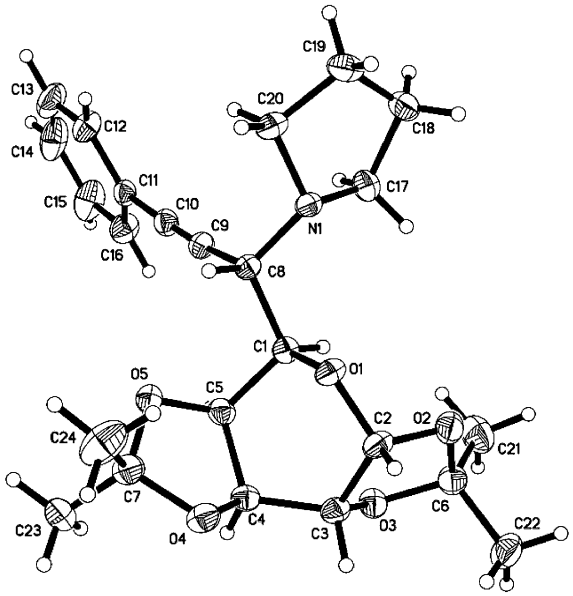


Figure 3. X-ray crystal structure of **6d**.

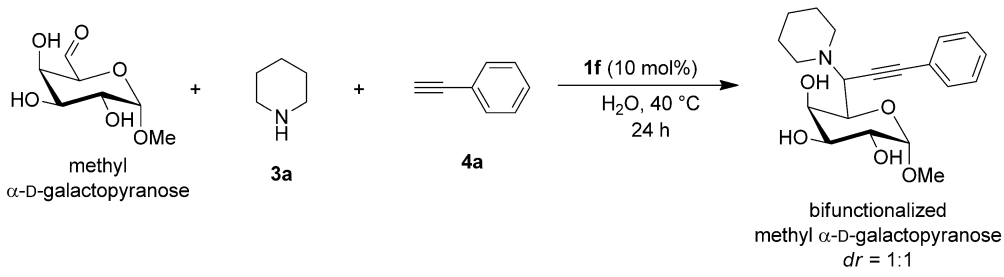
Supporting Information). In addition, good yields (64–75%) and excellent *dr* (96:4) were attained in coupling with amines and 4-ethynylanisole **4b** and 1-chloro-4-ethynylbenzene **4c** (entries 2, 3, 5 and 6).

To demonstrate the generality of this gold(III)-catalyzed reaction, the coupling reactions of aldehyde **2h**, pyrrolidine **3g** and arylacetylenes **4d–f** were examined and the corresponding propargylic amine-modified sugars **6g–i** with up to 65% yields and *dr* values up to 96:4 (Table 3, entries 7–9) were obtained. Notably, the hydroxy, amino and alkynyl moieties of **6g–i** remained intact, these functionalities in principle can be amenable for further organic transformation reactions, such as esterification, amide formation and azide-alkyne click reaction, respectively.

We found that both chiral aldehydes and amines have significant effects on the diastereoselectivity. As depicted in Table 3, **6a–i** with high diastereoselectivities (up to 97:3) were obtained (entries 1–9). The *dr* values (58:42 and 70:30) of **6j** and **6k** were significantly lowered when the L-prolinol amine derivatives **3b** and **3c** were used (Table 3, entries 1 and 2). High *dr* (up to 97:3) values of **6l** and **6m** were observed when using chiral D-prolinol amine components **3d** and **3e** of opposite absolute configurations (entries 3 and 4). With sterically bulky diphenyl L-prolinol **3f**, excellent yet inverted diastereoselectivity of 1:>99 (different from that obtained in **6a–i**, **6l** and **6m**) was observed in **6n** (entry 5).

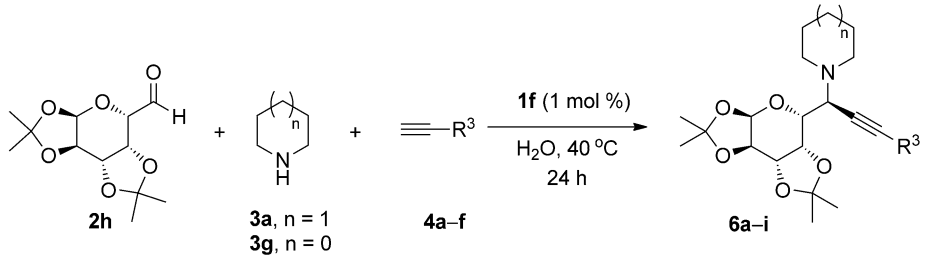
In order to explain the difference in diastereoselectivities observed for the three-component coupling of chiral sugar aldehydes with amines and alkynes, the following transition state models are proposed on the basis of the X-ray crystallographic structures of propargylic amine-modified sugars (Figure S2, Supporting Information).

The coupling reaction of sugar aldehyde **2h**, pyrrolidine **3g** and phenylacetylene **4a** is used as the first example (Table 3, entry 4). The two possible conformations (**A** and **B**) of the iminium salt generated by condensation of **2h** and **3g** are depicted in Scheme 3. Considering conformation **A**, the presence of an *O*-isopropylidene group of sugar aldehyde exerts steric hindrance to the pyrrolidine ring of the amine, which



Scheme 2. Bifunctional modification of an aldehyde-containing methyl α-D-galactopyranose *via* a gold(III) complex **1f**-mediated three-component coupling reaction.

Table 3. 1f-catalyzed propargylic amine synthesis *via* three-component coupling reaction of 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose **2h**, amine **3a** or **3g**, and alkynes **4a–f**.[a]



Entry	Amine	Alkyne	Product	Isolated yield [%]	dr[b]
1[c]	**3a**, $n=1$	**4a**, $R^3=Ph$	**6a**, $R^3=Ph$	76	97:3
2	**3a**	**4b**, $R^3=p$-$MeOC_6H_4$	**6b**, $R^3=p$-$MeOC_6H_4$	71	96:4
3	**3a**	**4c**, $R^3=p$-ClC_6H_4	**6c**, $R^3=p$-ClC_6H_4	75	96:4
4[c]	**3g**, $n=0$	**4a**	**6d**,[d] $R^3=Ph$	60	97:3
5	**3g**	**4b**	**6e**, $R^3=p$-$MeOC_6H_4$	64	96:4
6	**3g**	**4c**	**6f**,[d] $R^3=p$-ClC_6H_4	64	96:4
7	**3g**	**4d**, $R^3=p$-$(CH_2OH)C_6H_4$	**6g**, $R^3=p$-$(CH_2OH)C_6H_4$	65	93:7
8	**3g**	**4e**, $R^3=p$-$NH_2C_6H_4$	**6h**, $R^3=p$-$NH_2C_6H_4$	54	93:7
9	**3g**	**4f**, $R^3=m$-(ethynyl)C_6H_4	**6i**, $R^3=m$-(ethynyl)C_6H_4	51	96:4

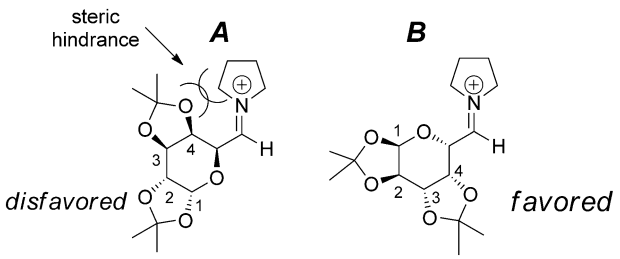
[a] *Reaction conditions:* catalyst **1f** (2 μmol), 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose **2h** (0.2 mmol), amine **3a** or **3g** (0.22 mmol) and alkyne **4a–f** (0.3 mmol) in water (1 mL).
[b] Determined by ^{1}H NMR analysis of crude reaction mixture.
[c] Catalyst **1f** (5 μmol), 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose **2h** (0.5 mmol), amine **3g** (0.55 mmol) and phenylacetylene **4a** (0.75 mmol).
[d] The absolute configuration determined by X-ray crystallography is shown in the Supporting Information.

is expected to be unfavorable. To avoid this steric hindrance, conformation **B** is expected to be more favorable.

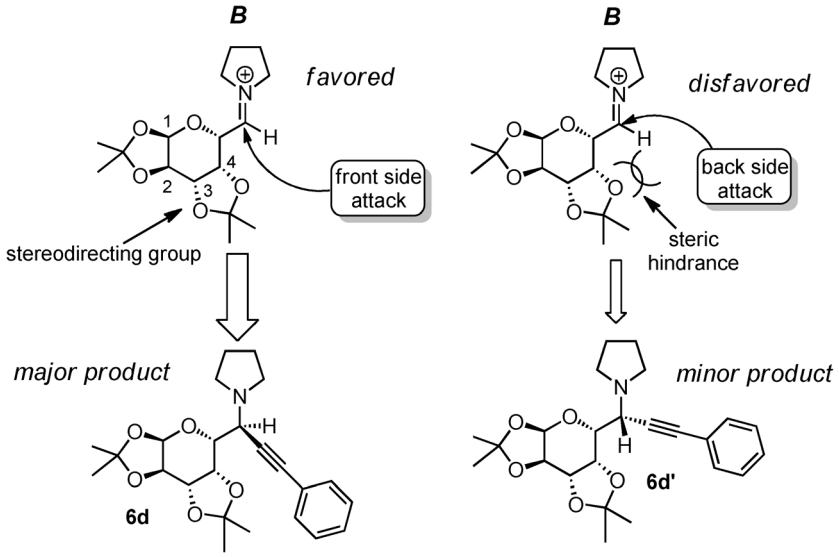
The conformation of the iminium salt intermediate determines the direction of nucleophilic attack of the gold acetylide (Scheme 4). Because of the steric hindrance exerted by the stereodirecting group at C-3 and C-4 positions of the sugar moiety, the back side attack by gold acetylide would be disfavored. The front side attack of the gold acetylide would be more favorable, giving propargylic amine-modified sugar **6d** as the major product ($dr=97:3$).

Poor diastereoselectivity ($dr=58:42$) was observed in the coupling of aldehyde **2h**, L-prolinol **3b** and phenylacetylene **4a** (Table 4, entry 1). This could be explained by the competitive steric effect induced by the α-substituent of L-prolinol (which disfavors the front side attack of the gold acetylide) and the stereodirecting group of the sugar moiety (which disfavors the back side attack of the gold acetylide), in which the latter gives a greater effect. Thus, the front side attack to the iminium intermediate by gold acetylide is slightly favored, giving diastereomers **6j** and **6j′** in a ratio of 58:42 (Scheme S3, Supporting Information). On the contrary, a synergetic steric effect was proposed for the formation of **6l** with high *dr* value of 97:3 (Table 4, entry 3), in which D-prolinol was used as the amine component instead of L-prolinol (Scheme S4, Supporting Information). The above rationale for the propargylic amine-modified sugars **6j** and **6l** (Table 4, entries 1 and 3) is also applicable to the methyl ether derivatives **6k** and **6m** (Table 4, entries 2 and 4).

Interestingly, the presence of diphenyl substituents on the α-substituent of L-prolinol lead to an overwhelming steric effect over the effect of stereodirecting groups on the sugar moiety. Thus, an excellent diastereoselectivity (1:>99) of **6n** (Table 4, entry 5) favoring the backside attack of the gold acetylide to the iminium intermediate was observed (Scheme S5, Supporting Information).

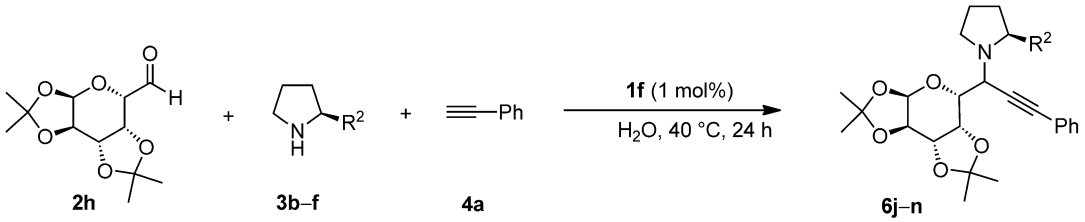


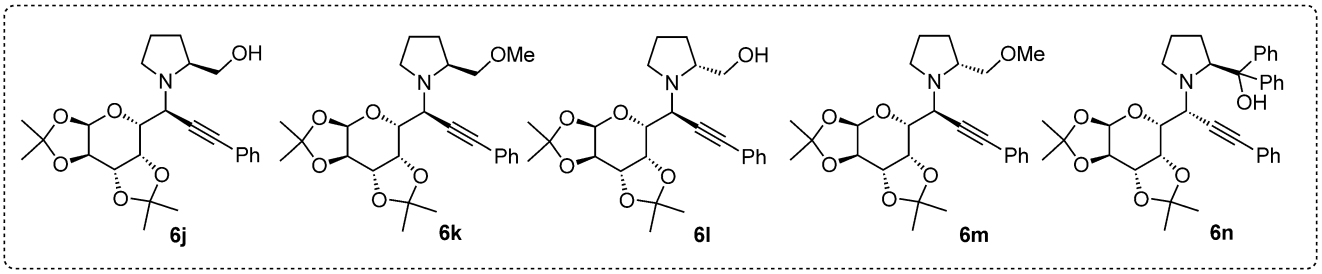
Scheme 3. Proposed structures of iminium salts.



Scheme 4. Proposed incoming direction of gold acetylide towards the formation of **6d**.

Table 4. The effect of chiral 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose **2h** and chiral amines **3b–f** on **1f**-catalyzed three component-coupling reactions.[a]





Entry	Amine	Alkyne	Product(s)	Isolated yield [%]	*dr*[b]
1	**3b**	**4a**	**6j**, **6j′**[c]	40, 30	58:42
2	**3c**	**4a**	**6k**, **6k′**	45, 15	70:30
3	**3d**	**4a**	**6l**	77	97:3
4	**3e**	**4a**	**6m**[c]	64	95:5
5	**3f**	**4a**	**6n**[c]	71	1:>99

[a] *Reaction conditions:* catalyst **1f** (2 μmol), 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose **2h** (0.2 mmol), amine **3b–f** (0.22 mmol) and phenylacetylene **4a** (0.3 mmol) in water (1 mL).
[b] Determined by ^{1}H NMR analysis of crude reaction mixture.
[c] The absolute configuration determined by X-ray crystallography is shown in the Supporting Information.

Synthesis of Chiral Allenes

Allenes are versatile synthetic intermediates in organic synthesis and structural elements of bioactive natural products and pharmaceutical compounds.[26] Current approaches for allene synthesis include S_N2' substitution of propargylic alcohols by organometallic reagents, 3,3-sigmatropic rearrangement, and asymmetric catalysis.[27] Allene synthesis can also be achieved by gold-catalyzed reactions under mild reaction con-

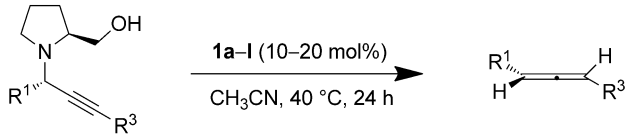
ditions.[28] In 2008, we discovered that $KAuCl_4$[11d] and $AgNO_3$[29] were effective catalysts to promote the synthesis of chiral allenes from chiral propargylic amines *via* 1,5-hydride shift in excellent enantioselectivities (up to 97% *ee*).

In the present work, we have found that cyclometallated gold(III) complexes were able to promote this reaction. Screening experiments were conducted by heating gold(III) complex **1a–l** (0.01–0.02 mmol, 10–20 mol%) and propargylic amine **5b** (0.1 mmol) in CH_3CN (2 mL) at 40 °C for 24 h, giving an enantioenriched allene (*R*)-**7a** in 86–98% *ee* (Table 5, entries 1–13). The results also revealed that the catalytic activities of the gold complexes with six-membered rings (entries 6–13) were better than that with five-membered rings (entries 1–5). Furthermore, attempt to increase the loading of **1f** from 10 to 20 mol% gave enhanced conversion (entry 6 *vs.* 7).

We further expanded the scope of this allene synthesis by using various propargylic amines. Using **5d** with the opposite chirality of **5b** as the substrate, allene (*S*)-**7a** was obtained in 91% *ee* (entry 14). High enantioselectivities (81–83% *ee*) were found in (*R*)-**7b** and (*R*)-**7c** having electron-rich alkyl moieties (entries 15–17). Propargylic amines with electron-withdrawing groups such as *p*-Cl (**5m** and **5h**) or *p*-Br (**5n**) gave the corresponding allenes (*R*)-**7e** and (*R*)-**7f** in excellent enantioselectivity (92–98% *ee*, entries 18–20).

Typically, chiral allenes are susceptible to racemization in the presence of transition metals and this restricts the use of chiral allenes in organic synthesis.[28a,29,30] We found that $KAuCl_4$ could be used as an effective catalyst for the highly enantioselective synthesis of chiral allenes (up to 97% *ee*) *via* 1,5-hydride shift of propagylic amines.[11d] Yet, electron-rich propargylic amines leading to the corresponding allenes with low enantioselectivities were reported. This observation could be explained by the coordination of $KAuCl_4$ to axially chiral allenes, resulting in racemization. Note that the substrate conversion with $AgNO_3$

Table 5. Cyclometallated gold(III) complex-catalyzed synthesis of chiral allenes.[a]

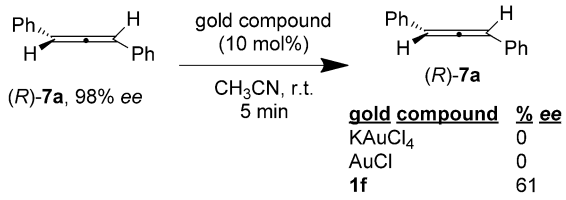


5b–d, 5h or **5j–n**
99% *ee*

7a–f
81–98% *ee*

Entry	Substrate	Product	Catalyst [mol%][b]	Conversion [%][c]	Yield [%][d]	*ee* [%][e]
1	**5b**	(*R*)-**7a**, R^1 = Ph, R^3 = Ph	**1a** (10)	10	68	92
2	**5b**	(*R*)-**7a**	**1b** (10)	20	80	86
3	**5b**	(*R*)-**7a**	**1c** (10)	10	70	94
4	**5b**	(*R*)-**7a**	**1d** (10)	5	trace	90
5	**5b**	(*R*)-**7a**	**1e** (10)	22	80	94
6	**5b**	(*R*)-**7a**	**1f** (10)	21	90	92
7	**5b**	(*R*)-**7a**	**1f** (20)	42	76	92
8	**5b**	(*R*)-**7a**	**1g** (10)	28	70	94
9	**5b**	(*R*)-**7a**	**1h** (10)	36	75	98
10	**5b**	(*R*)-**7a**	**1i** (10)	52	99	90
11	**5b**	(*R*)-**7a**	**1j** (10)	59	66	98
12	**5b**	(*R*)-**7a**	**1k** (10)	60	90	92
13	**5b**	(*R*)-**7a**	**1l** (10)	57	86	92
14	**5d**	(*S*)-**7a**	**1f** (20)	40	85	91
15	**5j**	(*R*)-**7b**, R^1 = *p*-MeC_6H_4, R^3 = Ph	**1f** (20)	20	80	81
16	**5k**	(*R*)-**7c**, R^1 = *p*-EtC_6H_4, R^3 = Ph	**1f** (20)	15	80	83
17	**5l**	(*R*)-**7d**, R^1 = *p*-(*i*-Pr)C_6H_4, R^3 = Ph	**1f** (20)	20	90	82
18	**5m**	(*R*)-**7e**, R^1 = *p*-ClC_6H_4, R^3 = Ph	**1f** (20)	5	trace	98
19	**5n**	(*R*)-**7f**, R^1 = *p*-BrC_6H_4, R^3 = Ph	**1f** (20)	15	90	92
20	**5h**	(*R*)-**7e**	**1f** (20)	5	trace	98

[a] *Reaction conditions:* gold complex **1a–l** (10 or 20 μmol) and propargylic amine **5b–d**, **5h** or **5j–n** (0.1 mmol) in CH_3CN (2 mL).
[b] Catalyst loading is shown in parenthesis.
[c] Determined by ^1H NMR analysis of crude reaction mixture based on conversion.
[d] Isolated yield based on conversion.
[e] Determined by HPLC using Chiralcel-OD column.



Scheme 5. Racemization study of chiral allenes using various gold compounds.

as catalyst decreased from 91% to 50% when the reaction was conducted in the presence of light.[29a]

To demonstrate the advantage of using cyclometallated gold(III) complexes as catalysts for chiral allene synthesis, the following experiments were conducted. Complete racemization resulted after mixing (*R*)-**7a** (98% *ee*) with $KAuCl_4$ or AuCl in CH_3CN at room temperature for 5 min (Scheme 5). This result is consistent with the work reported by Toste, Widenhoefer, and Krause, showing that chiral allenes could be racemized by gold compounds.[28a,30] Note that chiral allene (*R*)-**7a** (61% *ee*) could be recovered after treatment of (*R*)-**7a** (98% *ee*) with **1f** at room temperature for 5 min. These findings suggest that the use of pyridine-based ligands can help to minimize the enantioselectivity loss of chiral allenes, rendering highly enantioselective synthesis and functionalization of chiral allenes possible.

Synthesis of Isoxazoles *via* Cycloisomerization of α,β-Acetylenic Oximes

Isoxazoles are heteroaromatic compounds that are commonly used as synthetic building blocks and can be found in natural products and pharmaceuticals.[31] However, their syntheses *via* [3+2]cycloaddition reactions of alkenes/alkynes with nitrile oxides,[32] and the reactions of hydroxylamine with 1,3-dicarbonyl compounds,[33] α,β-unsaturated carbonyl compounds[34] and α,β-unsaturated nitriles[35] are hampered by the use of stoichiometric amounts of reagents, strong acids/bases, high reaction temperatures, prolonged reaction times and poor regioselectivity. Thus, the development of new methods for isoxazole synthesis is of importance in organic chemistry.[36] Recent works include the use of $AuCl_3$ as catalyst for isoxazole synthesis,[36d–g] but the reactions usually require dried solvent systems, protection of an nitrogen or argon atmosphere and refluxing conditions in order to achieve high product yields.

As depicted in Table 6, screening experiments involving heating of gold(III) complexes **1a–l** (1 μmol, 1 mol%), AgOTf (2 μmol, 2 mol%) and oxime **8a** (0.1 mmol) in $MeOH/CH_2Cl_2$ (1:1, 2 mL) at room temperature for 2 h were performed to give isoxazole **9a** with good to excellent yields (55–96%, entries 1–12). $AuCl_3$/AgOTf and Ph_3PAuCl/AgOTf were also found to be catalytically active, giving **9a** in 96% and 23% yields, respectively (entries 13 and 14). No reaction was observed in the control experiments with either catalyst **1f**, Ph_3PAuCl or AgOTf (entries 15–17).

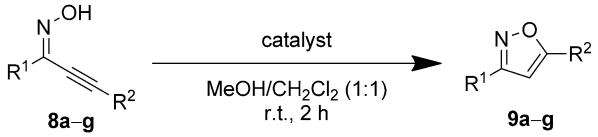
In some literature reports, gold ion was suggested to act as a proton source in homogeneous gold catalysis.[37] Some of the gold-catalyzed reactions were also found to be catalyzed by Brønsted acids.[38] Therefore, control experiments using Brønsted acids as an acid catalyst were set up to elucidate the role of the gold species in this reaction. Sulfuric acid, hydrochloric acid, methanesulfonic acid and trifluoroacetic acid gave 36–66% yields (entries 18–21). In general, using the cyclometallated gold(III) complexes as catalysts gave higher yields than Brønsted acids.

The generality of **1f**/AgOTf for the synthesis of isoxazoles was further demonstrated from the reaction of various aryl- and alkyl-substituted oximes. We have examined the effect on the yield of varying the nature of the R^1 group, while retaining R^2 as a phenyl group. Oximes with *p*-MeC_6H_4 (**8b**) and *m*-$MeOC_6H_4$ (**8c**) as the R^1 group gave isoxazoles **9b** and **9c** with excellent isolated yields (98–99%, entries 22 and 23), while a 70% yield was observed for isoxazole **9d**, which contains the bulky *tert*-butyl moiety as the R^1 group (entry 24). Oximes bearing phenyl rings with electron-donating (**8e**, *p*-MeO) and electron-deficient (**8f**, *p*-Br) groups in the R^2 group gave 70% isolated yields (entries 25 and 26). The reaction also works well for oxime **8g** with an *n*-butyl group in 98% isolated yield (entry 27). The present reaction could be conducted under mild reaction conditions without protection from nitrogen or argon atmosphere and dried solvent systems. Therefore, the cyclometallated gold(III) complexes **1a–l** prove to be effective catalysts for the transformation of α,β-acetylenic oximes to isoxazoles.

Synthesis, Characterization and Catalytic Activity of PEG-Linked Gold(III) Cyclometallated Complexes

The design and synthesis of polymer-supported transition metal catalysts continue to be a topic of immense interest.[39] As a model compound for the pursuit of PEG-supported gold catalysis, we found that *O*-benzyloxime-linked cyclometallated gold(III) complex **1l** exhibited excellent catalytic activity in the synthesis of propargylic amines, chiral allenes and isoxazoles as described in the previous sections. In this connection, PEG-linked hydroxylamine **10f** (av. MW = 500) was prepared from a coupling reaction of PEG-linked amine **10d**[40] and (Boc-aminooxy)acetic acid *N*-hydroxysuccinimide ester **11**[41] to give compound **10e**, followed by deprotection of the *tert*-butyloxycarbonyl

Table 6. Gold(III) cyclometallated complex-catalyzed synthesis of isoxazoles.[a]



Entry	Substrate	Product	Catalyst [mol%][b]	Isolated Yield [%]
1	**8a**, R^1 = Ph, R^2 = Ph	**9a**, R^1 = Ph, R^2 = Ph	**1a** (1)/AgOTf (2)	90
2	**8a**	**9a**	**1b** (1)/AgOTf (2)	88
3	**8a**	**9a**	**1c** (1)/AgOTf (2)	70
4	**8a**	**9a**	**1d** (1)/AgOTf (2)	60
5	**8a**	**9a**	**1e** (1)/AgOTf (2)	76
6	**8a**	**9a**	**1f** (1)/AgOTf (2)	60
7	**8a**	**9a**	**1g** (1)/AgOTf (2)	90
8	**8a**	**9a**	**1h** (1)/AgOTf (2)	55
9	**8a**	**9a**	**1i** (1)/AgOTf (2)	80
10	**8a**	**9a**	**1j** (1)/AgOTf (2)	86
11	**8a**	**9a**	**1k** (1)/AgOTf (2)	66
12	**8a**	**9a**	**1l** (1)/AgOTf (2)	96
13	**8a**	**9a**	$AuCl_3$ (1)/AgOTf (2)	96
14	**8a**	**9a**	Ph_3PAuCl (1)/AgOTf (2)	23
15	**8a**	**9a**	**1f** (1)	–[c]
16	**8a**	**9a**	Ph_3PAuCl (1)	–[c]
17	**8a**	**9a**	AgOTf (2)	–[c]
18	**8a**	**9a**	H_2SO_4 (1)	66
19	**8a**	**9a**	HCl (1)	46
20	**8a**	**9a**	CH_3SO_3H (1)	64
21	**8a**	**9a**	CF_3COOH (1)	36
22	**8b**, R^1 = *p*-MeC_6H_4, R^2 = Ph	**9b**, R^1 = *p*-MeC_6H_4, R^2 = Ph	**1f** (1)/AgOTf (2)	98
23	**8c**, R^1 = *m*-$MeOC_6H_4$, R^2 = Ph	**9c**, R^1 = *m*-$MeOC_6H_4$, R^2 = Ph	**1f** (1)/AgOTf (2)	99
24	**8d**, R^1 = *t*-Bu, R^2 = Ph	**9d**, R^1 = *t*-Bu, R^2 = Ph	**1f** (1)/AgOTf (2)	70
25	**8e**, R^1 = Ph, R^2 = *p*-$MeOC_6H_4$	**9e**, R^1 = Ph, R^2 = *p*-$MeOC_6H_4$	**1f** (1)/AgOTf (2)	70
26	**8f**, R^1 = Ph, R^2 = *p*-BrC_6H_4	**9f**, R^1 = Ph, R^2 = *p*-BrC_6H_4	**1 f** (1)/AgOTf (2)	70
27	**8g**, R^1 = Ph, R^2 = *n*-Bu	**9g**, R^1 = Ph, R^2 = *n*-Bu	**1f** (1)/AgOTf (2)	98

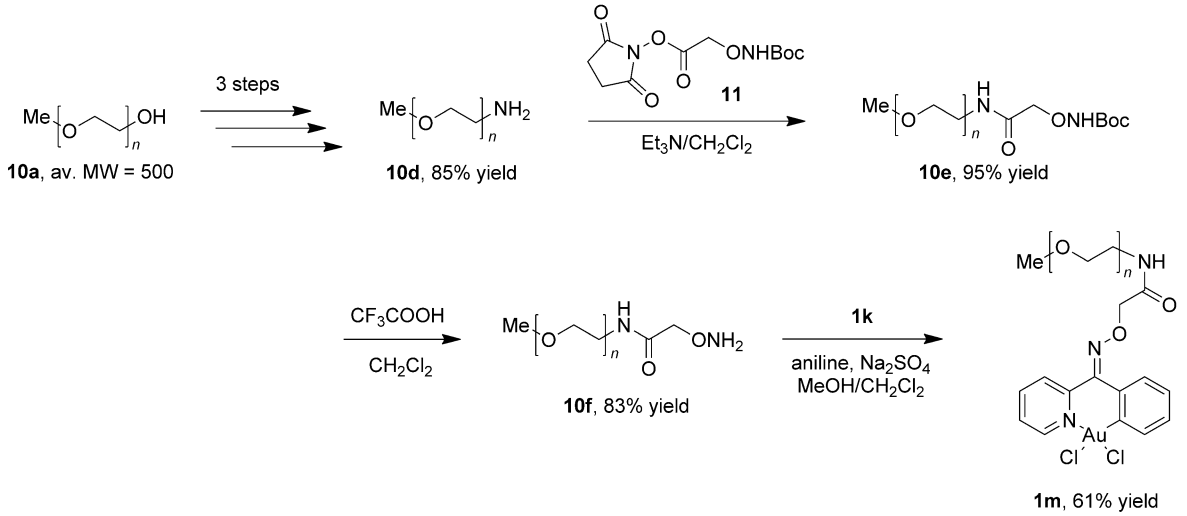
[a] *Reaction conditions:* catalyst and oxime **8a–g** (0.1 mmol) in MeOH/CH_2Cl_2 (1:1, 2 mL).
[b] Catalyst loading is shown in parenthesis.
[c] "–" = no reaction.

(Boc) group (Scheme 6). Through aniline-catalyzed oxime reaction of complex **1k** with compound **10f**, a PEG-linked cyclometallated gold(III) complex **1m** was prepared. The loading of the cyclometallated gold(III) complex in **1m** was 0.8 mmol g^{-1}, as determined by ^{1}H NMR analysis using the PEGCH_2O*Me* signal at *ca.* δ = 3.38 for the internal reference. After flash column chromatography, **1m** was obtained as a brown viscous liquid in 61% yield. Consistent with the properties of polyethylene glycol compounds, complex **1m** is insoluble in *n*-hexane and diethyl ether but highly soluble in ethyl acetate, dichloromethane and methanol. No significant change in the ^{1}H NMR spectrum of **1m** was found after storage in a vacuum dessicator for 30 days (Scheme S6, Supporting Information).

We evaluated the catalytic activity of **1m** towards the gold(III)-catalyzed organic reactions. In the gold(III)-catalyzed three-component coupling reaction, this PEG-supported catalyst **1m** afforded a product turnover of 900.

We then examined the recyclability of catalyst **1m**, and the experiments were conducted with **1m** (10 μmol, 1 mol%), benzaldehyde **2a** (1 mmol), piperidine **3a** (1.1 mmol) and phenylacetylene **4a** (1.5 mmol) in water at 40 °C under air. After 24 h, the substrate conversion based on benzaldehyde was determined by ^{1}H NMR analysis of an aliquot of reaction mixture taken out from the reaction flask. An additional portion of starting materials was added into the reaction mixture. The reaction was continued for an additional 24 h. As depicted in Table 7, PEG-linked cyclometallated gold(III) complex **1m** could be repeatedly used for 12 cycles leading to product turnovers of 872 in total.

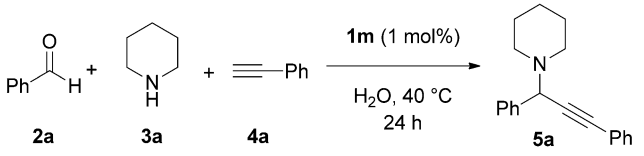
Some of the substrates described in previous sections were selected for catalysis screening experiments with PEG-linked complex **1m** as catalyst. All



Scheme 6. Synthetic scheme of PEG-linked cyclometallated gold(III) complex **1m**.

the substrates gave the corresponding products with yields that were comparable to or better than those obtained using complexes **1f**, **1k** or **1l** as catalyst. Propargylic amine **5p** was obtained in 60% yield (Table 8, entry 1), while **5b**, **5g** and **5h** were obtained in good to excellent yields (56–80%) with excellent distereoselectivities (entries 2–4). For chiral sugar-based aldehyde **2h**, the *dr* values of proparylic amines **6d** and **6j** were found to be 93:7 and 55:45, respectively (entries 5 and 6). Chiral allenes (*R*)-**7a**, **7c** and **7e** were obtained in good substrate conversions, yields and with excellent enantioselectivities (82–92% *ee*, entries 7–9). Isoxazoles **9a**, **9d** and **9f** were obtained in 64–77% isolated yields (entries 10–12).

Table 7. Experiment on the recycling of PEG-linked gold(III) complex **1m** in the synthesis of propargylic amines.[a]



Cycle	Conversion [%][b]	Cycle	Conversion [%][b]
1	90	7	74
2	74	8	70
3	70	9	78
4	73	10	70
5	70	11	70
6	72	12	61

[a] *Reaction conditions:* catalyst **1m** (10 μmol), benzaldehyde **2a** (1 mmol), piperidine **3a** (1.1 mmol) and phenylacetylene **4a** (1.5 mmol) in water (1 mL).

[b] Determined by ^{1}H NMR analysis of crude reaction mixture based on benzaldehyde conversion.

Conclusions

We have synthesized a series of cyclometallated gold(III) complexes **1a**–**l** and a PEG-linked complex **1m**. These gold(III) complexes were found to be active catalysts for the synthesis of propargylic amines, chiral allenes and isoxazoles. Our findings highlight the prospect of the potential of using cyclometallated gold(III) complexes as catalysts in organic transformation reactions.

Experimental Section

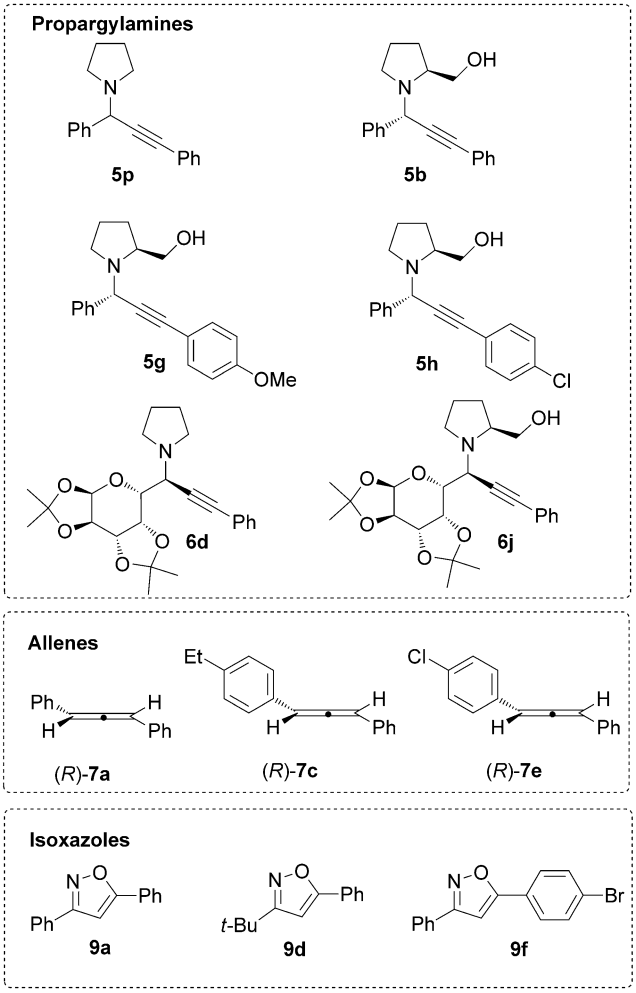
General Procedure for Synthesis of Cyclometallated Gold(III) Complexes 1c–d *via* Transmetallation

Arylpyridine (**1ca** or **1da**, 5 mmol) in EtOH (20 mL) was added slowly to a stirred solution of $Hg(OAc)_2$ (1.6 g, 5 mmol) in EtOH (20 mL). The mixture was refluxed for 12 h and hot filtered into a solution of LiCl (212 mg, 5 mmol) in MeOH (20 mL). This mixture was refluxed for 1 h and allowed to cool overnight. The precipitate was filtered off, washed with H_2O (50 mL) to give an organomercury intermediate (**1cb** or **1db**). The corresponding organomercury intermediate (**1cb** or **1db**, 0.2 mmol) in CH_2Cl_2 (8 mL) was added to a solution of $KAuCl_4$ (76 mg, 0.2 mmol) in CH_3CN, and the mixture was stirred at room temperature for 12 h. A cyclometallated gold(III) complex (**1c** or **1d**) was separated and washed with CH_3CN and dried under air; yields of **1c**: 20% and **1d**: 94%.

Procedure for Synthesis of Cyclometallated Gold(III) Complexes 1h and 1j by Direct Auration Reaction

Arylpyridine (**1ha** or **1ja**, 1 mmol) and $KAuCl_4$ (0.378 g, 1 mmol) were mixed and stirred in CH_3CN/H_2O (1:4, 20 mL) at room temperature for 1 h. The resulting mixture

Table 8. PEG-linked gold(III) complex **1m**-catalyzed organic reactions.[a]



Entry	Substrate(s)	Product(s)	Yield [%][b]
1	**2a**, **3g**, **4a**	**5p**	60
2	**2a**, **3b**, **4a**	**5b**	80 (94:6)
3	**2a**, **3b**, **4b**	**5g**	80 (92:8)
4	**2a**, **3b**, **4c**	**5h**	56 (94:6)
5	**2b**, **3g**, **4a**	**6d**	50 (93:7)
6	**2b**, **3b**, **4a**	**6j**	30 (55:45)
		6j′	25
7[c]	**5b**	(*R*)-**7a**	75 [20] (90% *ee*)
8[c]	**5k**	(*R*)-**7c**	50 [15] (82% *ee*)
9[c]	**5h**	(*R*)-**7e**	40 [12] (92% *ee*)
10	**8a**	**9a**	73
11	**8d**	**9d**	77
12	**8f**	**9f**	64

[a] Reaction conditions were similar to that in Tables 2–6, but with complex **1m** as the catalyst.
[b] Conversion is shown in square brackets; diastereomeric ratio/enantioselectivity is shown in parenthesis.
[c] Complex **1m** (10 mol%) was used.

was then filtered and washed with H_2O and diethyl ether to give *N*-bonded gold(III) intermediate (**1hb** or **1jb**). *N*-Bonded gold(III) intermediate (**1hb** or **1jb**, 0.2 mmol) was then refluxed in CH_3CN/H_2O (1:5, 20 mL) overnight until a precipitate was formed. The precipitate was filtered and washed with diethyl ether and H_2O to give cyclometallated gold(III) complex (**1h** or **1j**) as a product; yields of **1h**: 17% and **1j**: 24%.

General Procedure for Synthesis of Cyclometallated Gold(III) Complex 1l *via* Aniline-Catalyzed Oxime Ligation

To a solution of **1k** (23 mg, 0.05 mmol), *O*-benzylhydroxylamine hydrochloride and anhydrous Na_2SO_4 (100 mg) in $MeOH/CH_2Cl_2$ (1:4, 5 mL) was added pyridine (4 μL, 0.05 mmol). The mixture was stirred at room temperature for 18 h. After the reaction, the mixture was filtered and evaporated to approximately 2 mL by a rotary drier. Diethyl ether (20 mL) was added into the mixture to precipitate a white solid which was collected by vacuum filtration and washed with diethyl ether to give the product as a white powder; yield of **1l**: 72%.

Catalytic Activities of Cyclometallated Gold(III) Complex-Catalyzed Synthesis of Propargylic Amines *via* Three-Component Coupling Reaction

A mixture of cyclometallated gold(III) complex **1a**–**l** (2 μmol), benzaldehyde **2a** (200 μL, 2 mmol), piperidine **3a** (220 μL, 2.2 mmol) and phenylacetylene **4a** (330 μL, 3 mmol) in water (1 mL) was stirred at 40 °C for 24 h. The reaction mixture was extracted with diethyl ether. The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The turnover number was then determined from the isolated yield of product based on benzaldehyde conversion in ^{1}H NMR analysis of the crude reaction mixture.

Cyclometallated Gold(III) Complex-Catalyzed Synthesis of Propargylic Amines *via* Three-Component Coupling Reaction

A mixture of cyclometallated gold(III) complex **1a**–**l** (5 μmol), aldehyde **2a**–**g** (0.5 mmol), amine **3b**–**f** (0.55 mmol) and alkyne **4a**–**d** (0.75 mmol) in water (1 mL) was stirred at 40 °C for 24 h. The reaction mixture was extracted with diethyl ether. The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Propargylic amine **5a**–**o** was purified by flash column chromatography on silica gel using *n*-hexane/EtOAc as eluent.

General Procedure for Cyclometallated Gold(III) Complex-Catalyzed Three-Component Coupling Reaction for 1,2:3,4-Di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-l,5-pyranose Aldehyde with Various Amines and Alkynes

A mixture of cyclometallated gold(III) complex **1f** (1 mg, 2 μmol), 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-l,5-pyranose aldehyde **2h** (52 mg, 0.2 mmol), amine **3a**–**g** (0.22 mmol) and alkyne **4a**–**f** (0.3 mmol) in water (1 mL) was stirred at 40 °C for 24 h. The reaction mixture was extracted with diethyl ether. The combined organic layers

were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Propargylamine **6a–n** was purified by flash column chromatography on silica gel using *n*-hexane/EtOAc as eluent.

General Procedure for Cyclometallated Gold(III) Complex-Catalyzed Synthesis of Chiral Allenes

A mixture of propargylic amine **5b–d**, **5h** or **5j–n** (0.1 mmol) and cyclometallated gold(III) complex **1a–l** (10 or 20 μmol) in CH_3CN (2 mL) was stirred at 40 °C for 24 h. The reaction mixture was concentrated under reduced pressure. Allene **7a–f** was purified by flash column chromatography on silica gel using *n*-hexane/EtOAc as eluent. The enantioselectivitis of chiral allenes (*R*)-**7a**, (*S*)-**7a** and (*R*)-**7b–f** were determined by HPLC using Chiralcel-OD column using *n*-hexane/isopropyl alcohol as eluent.

General Procedure for Racemization Study of Chiral Allene (*R*)-7a

A mixture of allene (*R*)-**7a** (98% *ee*, 19 mg, 0.1 mmol) and cyclometallated gold(III) complex **1f** (4 mg, 10 μmol) in CH_3CN (2 mL) was stirred at room temperature for 5 min. A portion (50 μL) of the reaction mixture was pipetted and purified through a glass dropper packed with silica gel using *n*-hexane/EtOAc as eluent. The enantioselectivity was determined by HPLC using Chiralcel-OD column using *n*-hexane/isopropyl alcohol as eluent. The above experiment was repeated for $KAuCl_4$ and AuCl.

General Procedure for Cyclometallated Gold(III) Complex-Catalyzed Synthesis of Isoxazoles

A mixture of α,β-unsaturated oxime **8a–g** (0.1 mmol), cyclometallated gold(III) complex **1a–l** (1 μmol) and AgOTf (2 μmol, 2 mol%) in $MeOH/CH_2Cl_2$ (1:1, 2 mL) was stirred at room temperature for 2 h. The crude reaction mixture was concentrated under reduced pressure. Isoxazole **9a–g** was purified by flash column chromatography on silica gel using *n*-hexane/diethyl ether as eluent.

Procedure for Synthesis of PEG-Linked Cyclometallated Gold(III) Complex 1m

A mixture of aminooxy compound **10f** (58 mg, 0.1 mmol) and complex **1k** (45 mg, 0.1 mmol) was dissolved in CH_2Cl_2 (10 mL). Aniline (14 μL, 0.15 mmol) and $MgSO_4$ (100 mg, 0.83 mmol) were then added into the mixture. The resulting mixture was stirred at room temperature for 12 h. After finishing the reaction, the mixture was filtered and concentrated to dryness under reduced pressure. The product was purified by flash column chromatography on silica gel using $MeOH/CH_2Cl_2$ as eluent to afford PEG-linked cyclometallated gold(III) complex **1m**; yield: 61%. The loading of cyclometallated gold(III) complex was determined by ^1H NMR using the $PEGCH_2OMe$ signal at ca. $\delta = 3.38$ as internal standard.

Catalytic Activity of PEG-Linked Cyclometallated Gold(III) Complex 1m-Catalyzed Synthesis of Propargylic Amines *via* Three-Component Coupling Reaction

A mixture of cyclometallated gold(III) complex **1m** (1 μmol), benzaldehyde **2a** (200 μL, 2 mmol), piperidine **3a** (220 μL, 2.2 mmol) and phenylacetylene **4a** (330 μL, 3 mmol) in water (1 mL) was stirred at 40 °C for 24 h. The reaction mixture was extracted with diethyl ether. The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Turnover number was then determined by isolated yield of product based on benzaldehyde conversion in ^1H NMR analysis of the crude reaction mixture.

Recyclability of PEG-Linked Cyclometallated Gold(III) Complex 1m-Catalyzed Synthesis of Propargylic Amines *via* Three-component Coupling Reaction

A mixture of cyclometallated gold(III) complex **1m** (10 μmol), benzaldehyde **2a** (100 μL, 1 mmol), piperidine **3a** (110 μL, 1.1 mmol) and phenylacetylene **4a** (165 μL, 1.5 mmol) in water (1 mL) was stirred at 40 °C for 24 h. After 24 h, the substrate conversion based on benzaldehyde was determined by ^1H NMR analysis of an aliquot of reaction mixture taken out from the reaction flask. An additional portion of starting materials was added into the reaction mixture. The reaction was continued for an additional 24 h.

Crystal Structures

CCDC 918208 (**1j**), 918209 (**5o**), 918210 (**6d**), 918211 (**6f**), 918212 (**6j′**), 918213 (**6m**) and 918214 (**6n**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

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