

Gold(I)–Phosphine Catalyst for the Highly Chemoselective Dehydrogenative Silylation of Alcohols

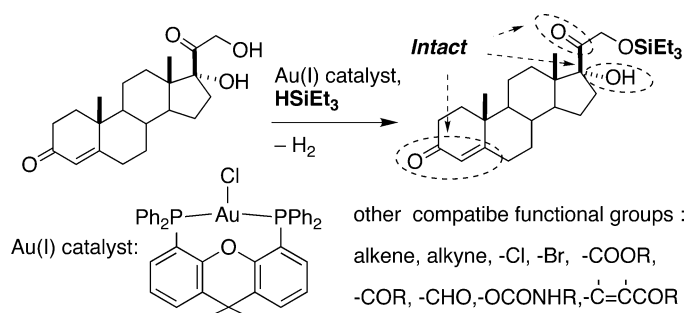
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Received April 30, 2005

ABSTRACT



A gold(I) complex of Xantphos AuCl(xantphos) catalyzes the dehydrogenative silylation of alcohols with high chemoselectivity and solvent tolerance. It is selective for the silylation of hydroxyl groups in the presence of alkenes, alkynes, alkyl halides (RCl, RBr), ketones, aldehydes, conjugated enones, esters, and carbamates.

The development of environmentally benign processes is an important subject in organic synthesis.¹ We have focused on the dehydrogenative silylation of hydroxy groups with hydrosilanes as a useful method with high atom efficiency.^{2–5} Recently, we reported that a Cu(I)–Xantphos catalyst is

remarkably active for the dehydrogenative silylation of alcohols with high selectivity.^{6,7} These studies revealed a strong ligand effect of Xantphos, which accelerates dehydrogenative silylation of alcohols.

Here, we report that a gold(I) complex of Xantphos catalyzes the dehydrogenative silylation of alcohols and

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Table 1. Ligand Effect in Au(I)-Catalyzed Dehydrogenative Silylation
$$\text{Ph-CH}_2\text{-CH}_2\text{-OH} + \text{HSiEt}_3 \xrightarrow[\text{50 } ^\circ\text{C, 2.5 h}]{\text{Au(I) catalyst (1 mol \%), ClCH}_2\text{CH}_2\text{Cl (0.5 mL)}} \text{Ph-CH}_2\text{-CH}_2\text{-OSiEt}_3 + \text{H}_2$$

(0.5 mmol) 2 equiv

entry	catalyst	yield ^a (%)
1	AuCl(SMe ₂)	11
2	Xantphos/AuCl(SMe ₂)	94
3	PPh ₃ /AuCl(SMe ₂)	trace
4	dppe/AuCl(SMe ₂)	0
5	dppp/AuCl(SMe ₂)	trace
6	dppb/AuCl(SMe ₂)	trace
7	dppf/AuCl(SMe ₂)	11
8	DPEphos/AuCl(SMe ₂)	5
9	DBFphos/AuCl(SMe ₂)	0
10	AuCl(PPh ₃) ₂ ^b	2
11 ^c	AuCl(xantphos) ^b	100

^a GC yield of the silyl ether. No side reaction occurred. ^b Isolated complex was used. ^c Yield after reaction for 2 h.

exhibits an unprecedented high chemoselectivity and solvent tolerance. The gold complex is selective for the silylation of hydroxy groups in the presence of other functional groups including alkenes, alkynes, alkyl halides (RCl, RBr), aldehydes, ketones, conjugated enones, esters, and carbamates, while its activity is somewhat milder than that of the Cu(I)–Xantphos catalyst. Furthermore, the reaction can be conducted in a variety of solvents. Use of the Xantphos ligand is essential for the catalytic activity of the gold complex. ³¹P NMR studies strongly suggest that a key feature of the Au(I) catalyst is the monomeric three-coordinated nature of the catalytically active species.

A series of Au(I)–phosphine catalysts prepared by mixing AuCl(SMe₂) with phosphines was screened (Table 1). Catalytic activity of the Au(I) complexes was determined by the yield of the silyl ether after reaction of 2-phenylethanol with HSiEt₃ at 50 °C for 2.5 h in the presence of 1 mol % of a catalyst precursor.⁸ Use of AuCl(SMe₂) as the catalyst without phosphine ligands resulted in a poor yield (11%) of the silyl ether, accompanied by precipitation of metallic gold early in the reaction (within 10 min) (entry 1). The Xantphos ligand performed significantly better than the other phosphine ligands including the monodentate (PPh₃) and bidentate (dppe, dppp, dppb, dppf, DPEphos,^{7a} and DBFphos^{7a,9}) phosphines, producing the silyl ether in 94% yield after 2.5 h without precipitation of metallic gold; the other ligands produced a yield of less than 11% (entries 2–9). Isolated AuCl(PPh₃)₂ furnished a low yield (2%) under identical conditions (entry 10). The isolated complex of AuCl(xantphos) was slightly more active than the catalyst gener-

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(8) See Supporting Information for detailed procedure.

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Table 2. AuCl(xantphos)-Catalyzed Dehydrogenative Silylation in Various Solvents
$$\text{Ph-CH}_2\text{-CH}_2\text{-OH} + \text{HSiEt}_3 \xrightarrow[\text{50 } ^\circ\text{C}]{\text{AuCl(xantphos) (1 mol \%), solvent (0.5 mL)}} \text{Ph-CH}_2\text{-CH}_2\text{-OSiEt}_3 + \text{H}_2$$

(0.5 mmol) 2 equiv

entry	solvent	time (h)	yield ^a (%)
1	CHCl ₃	3	99
2	ClCH ₂ CH ₂ Cl	2	100
3	acetone	5	98
4 ^b	DMF	2	100
5	NMP	5	99
6	DMSO	5	95
7	benzonitrile	5	98
8	CF ₃ C ₆ H ₅	5	91
9	toluene	5	56
10	<i>t</i> -BuOH	9.5	100
11	neat	24	76

^a GC yield of the silyl ether. No side reaction occurred. ^b After reaction was complete, Au(0) precipitation was observed.

ated in situ (entry 11, 100%, 2 h).^{10,11} The reactivity profile with ligands was similar to that obtained previously using Cu(I)–Xantphos.⁶ It should be noted, however, that the Au(I)–Xantphos activity was somewhat lower than that of Cu(I)–Xantphos.¹²

AuCl(xantphos) was effective in a broad range of reaction media, including coordinating solvents (results summarized in Table 2). Silylation of 2-phenylethanol with HSiEt₃ at 50 °C resulted in high yields (2–3 h, 99–100%) in halogenated solvents (CHCl₃, ClCH₂CH₂Cl: entries 1 and 2). Although ketones easily undergo hydrosilylation in the presence of various transition metal catalysts, the Au(I) catalyst demonstrated no hydrosilylation activity toward those substrates (vide infra). Therefore, acetone was a good solvent (entry 3). Few transition metal catalysts are active in polar solvents,^{3g,h} and the activity of some catalysts is strongly inhibited by coordinating solvents.^{3j,4b,d} Nevertheless, dehydrogenative silylation with Au(I) catalyst proceeded smoothly in amide solvents (DMF, NMP: entries 4, 5), DMSO (entry 6), and benzonitrile (entry 7). Silylation also proceeded smoothly in a fluorinated solvent, i.e., CF₃C₆H₅ (entry 8). Reaction in toluene resulted in a moderate yield due to low

(10) AuCl(xantphos) is stable to air and moisture, storable, and easy to handle. Detailed synthetic procedure and spectroscopic data are provided in Supporting Information. Lagunas et al. reported that a signal at 22.9 ppm observed in the titration of [(AuCl)₂(μ-xantphos)] with Xantphos in CDCl₃ corresponded to AuCl(xantphos). However, they did not isolate the AuCl(xantphos); see ref 11a. Although this complex is stable in the solid state for several weeks and in CHCl₃ for 1 day, partial disproportionation of AuCl(xantphos) to [(AuCl)₂(xantphos)₂] and [Au(xantphos)₂]Cl was observed in CH₂Cl₂.

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(12) Silylation of a primary alcohol with triethylsilane was completed within 1 h in the presence of Cu(I)–Xantphos at rt; see ref 6.

Table 3. AuCl(xantphos)-Catalyzed Dehydrogenative Silylation of Primary, Secondary, and Tertiary Alcohols^a

$$\text{ROH} + \text{HSiR}^1\text{R}^2\text{R}^3 \xrightarrow[\text{solvent}]{\text{cat. AuCl(xantphos)}} \text{ROSiR}^1\text{R}^2\text{R}^3 + \text{H}_2$$

entry	hydrosilane	alcohol	solvent	catalyst (mol %)	temp. (°C)	time (h)	yield ^b (%)
1	HSiEt ₃		acetone	1	50	6	98
2	HSiEt ₃		acetone	1	50	7	99
3	HSiEt ₃		ClCH ₂ CH ₂ Cl	3	80	12	98
4	HSiEt ₃		DMF	3	80	0.5	82
5	HSiMe ₂ Ph		ClCH ₂ CH ₂ Cl	1	50	1	98
6	HSiMe ₂ tBu		ClCH ₂ CH ₂ Cl	1	80	4	96
7	HSiMe ₂ tBu		DMF	5	80	4	95
8	HSiPh ₃		ClCH ₂ CH ₂ Cl	1	50	52	95
9	HSiPh ₂ tBu		DMF	5	80	95	93

^a Conditions: AuCl(xantphos) (1.0 mol %, 0.005 mmol) with an alcohol (0.5 mmol), hydrosilane (1.0 mmol), and solvent (0.5 mL) at 50 °C. ^b Isolated yield.

solubility of the Au(I)–Xantphos catalyst (entry 9). Even *tert*-butyl alcohol could be used as a solvent. Only a trace amount of the silyl ether of solvent was detected under the present conditions (entry 10). The Au(I) catalyst was effective even neat, although a longer reaction time was necessary to obtain a reasonable yield (24 h, 76%, entry 11).

The range of substrates for nonfunctionalized alcohols is presented in Table 3. Silylation of primary and secondary alcohols with HSiEt₃ proceeded smoothly in the presence of 1 mol % Au(I) catalyst at 50 °C (entries 1 and 2). A tertiary alcohol also was silylated with HSiEt₃ in the presence of 3 mol % of catalyst at 80 °C in dichloroethane (98%, entry 3). Silylation of a phenolic alcohol resulted in good yield of product (82%, entry 4). HSiMe₂Ph reacted smoothly with 1-phenylethanol to give the corresponding silyl ether in high yield (98%, entry 5). Reaction of HSiMe₂tBu with a primary or secondary alcohol proceeded at 80 °C, giving the corresponding silyl ether in high yields (entries 6 and 7). HSiPh₃ could be used for silylation of a primary alcohol (i.e., 2-phenylethanol) (entry 8). The bulky silyl reagent HSiPh₂tBu also reacted with a primary alcohol, giving the silyl ether in good yield (entry 9).

Functional group compatibility of the Au(I) catalyst is shown in Table 4. 9-Decen-1-ol and 10-undecyn-1-ol were converted to the corresponding silyl ethers without hydro-silylation of their unsaturated C–C bonds (entries 1 and 2). Silylation of 3-chloro- and 3-bromopropanol proceeded smoothly with the C–X bonds intact (entries 3 and 4). This gold(I) catalyst is applicable for substrates containing alde-

hydes and conjugated carbonyl moieties (entries 5 and 6).¹³ No dehydrogenative silylation catalyst compatible with such a wide range of functional groups has been reported.^{3–6}

Table 4. AuCl(xantphos)-Catalyzed Dehydrogenative Silylation of Functionalized Alcohols^a

$$\text{FG-ROH} + \text{HSiEt}_3 \xrightarrow[\text{solvent, 50 } ^\circ\text{C}]{\text{cat. AuCl(xantphos)}} \text{FG-ROSiR}_3 + \text{H}_2$$

entry	product	solvent	time (h)	yield ^b (%)
1		acetone	8	100
2		ClCH ₂ CH ₂ Cl	4.5	97
3		ClCH ₂ CH ₂ Cl	2.5	95
4		ClCH ₂ CH ₂ Cl	52	86
5		ClCH ₂ CH ₂ Cl	2	98
6 ^c		ClCH ₂ CH ₂ Cl	5	80
7		DMF / CHCl ₃	6	96
8 ^d		DMF	2	97

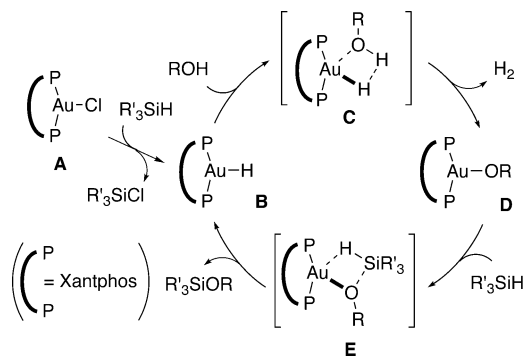
^a Conditions: AuCl(xantphos) (1.0 mol %, 0.005 mmol) with an alcohol (0.5 mmol), hydrosilane (1.0 mmol), and solvent (0.5 mL) at 50 °C. ^b Isolated yield. ^c 3.0 mol % of catalyst was used. ^d 2.0 mol % of catalyst was used.

The reaction of cortexolone containing a primary and a tertiary hydroxy group, conjugated enone, and isolated ketone moiety resulted in selective dehydrogenative silylation of the primary hydroxy group (entry 7). *N*-Boc-D-serine methyl ester was converted to the corresponding silyl ether without racemization (entry 8).

Among the ligands, only Xantphos gave a sharp singlet $^3\text{P}\{^1\text{H}\}$ NMR signal (28.8 ppm) upon treatment with AuCl(SMe₂), corresponding to the monomeric three-coordinated complex (AuX(P–P)). It is noteworthy that three-coordinated complexes of AuX chelated with diphosphines are very rare.^{14,15} All phosphines tested gave broad or multiple resonances, attributable to polymeric complexes $[\{\text{AuX}(\text{P}–\text{P})\}_n]$, two-coordinated linear complexes $[(\text{AuX})_2(\text{P}–\text{P})]$, three-coordinated annular complexes $[(\text{AuX})_2(\text{P}–\text{P})_2]$ or four-coordinated cationic complexes $[(\text{Au}(\text{P}–\text{P})_2^+)]\text{X}^-$.^{16,17} Mass spectrum analysis (ESI) of AuCl(xantphos) supported the assignment for the monomeric structure ($m/z = 775.1568$ $[\text{M} – \text{Cl}]^+$).

A possible mechanism is depicted in Scheme 1. The reaction of AuCl(xantphos) (**A**) with a hydrosilane generates

Scheme 1. Proposed Mechanism for Au(I)–Xantphos-Catalyzed Dehydrogenative Silylation



Au(I) hydride **B** and the corresponding chlorosilane. The Au(I) hydride **B** reacts with an alcohol through σ -bond metathesis involving transition state **C** to afford alkoxogold(I) derivative **D** and molecular hydrogen. Then, σ -bond metathesis (**E**) between the hydrosilane and alkoxogold(I) **D** affords the silyl ether with regeneration of Au(I) hydride **B**. The superiority of the Xantphos ligand prompted us to propose: (1) The monomeric structure is essential for each metathesis reaction. Xantphos is suitable for formation of a three-coordinated monomeric complex with Au(I) metal.¹⁴ (2) Large P–Au–P bite angles induced by Xantphos activate the Au–X (X = Cl, H, OR) bonds.^{14a}

In summary, Au(I)–Xantphos is a useful catalyst for dehydrogenative silylation of alcohols. Its benefits include the ability to function in a broad range of solvents, and high functional group compatibility. We propose that the strong ligand effect of Xantphos in this Au(I) catalyst system is due to its ability to form a three-coordinated monomeric structure. Efforts to improve catalytic activity and to gain mechanistic insights are continuing.

Acknowledgment. H.I. thanks Meiji Seika for generous financial support.

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

OL050979Z

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