

# Silver and gold reagents

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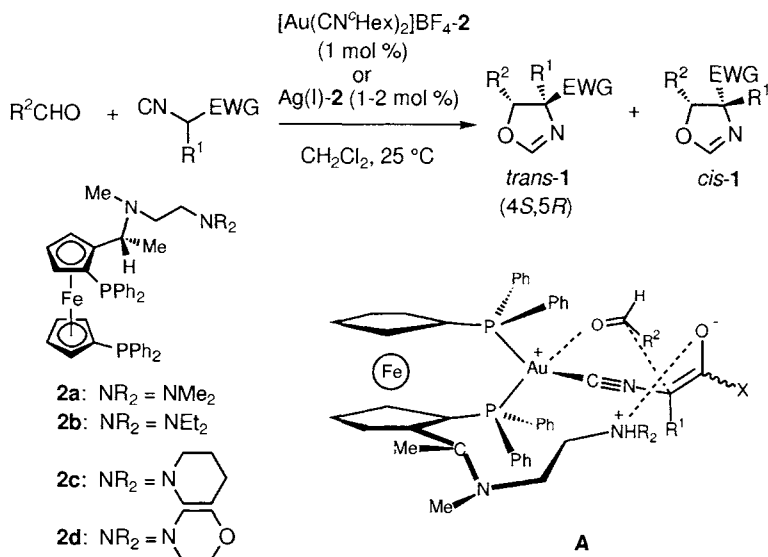
## 1. Introduction

Owing to their weak Lewis-acidity, reagents involving a silver(I) or gold(I) ion have attracted little attention as a Lewis-acid reagent to date. As described in this chapter, however, phosphine-co-ordinated silver(I) and gold(I) complexes have been successfully applied to the aldol-type condensation of isocyanides with aldehydes, where the silver(I) and gold(I) complexes activate the isocyanide through  $\eta^1$ -co-ordination of the isocyano carbon (see Section 2). Although these complexes show rather low affinity to an oxygen functional group such as a carbonyl group, an example of carbonyl group activation can be seen in the silver(I)-catalysed allylation of aldehydes with allyltin reagents as a Lewis acid catalyst (see Section 3).

## 2. Enantioselective aldol reaction of activated isocyanides and aldehydes

Aldol-type reaction of activated isocyanides with aldehydes are effectively catalysed by a gold(I) or silver(I) complex of a chiral bis(phosphino)ferrocene bearing an ethylenediaminoalkyl pendant, producing optically active oxazolines.<sup>1,2</sup> The activating group on the isocyanides includes an alkoxycarbonyl,<sup>3–20</sup> carbamoyl,<sup>21–23</sup> phosphonyl,<sup>24,25</sup> or sulfonyl group<sup>26</sup> (Scheme 9.1, Tables 9.1 and 9.2). The reaction catalysed by silver(I) complex requires a slow addition of the isocyanide (over 1 h) except for the reaction of tosylmethyl isocyanide.

In most cases, the *trans*-oxazoline is predominantly formed with a high enantioselectivity, whereas the *cis*-oxazoline with low enantiomeric excess is as a minor product. The *trans*-oxazolines can readily be converted into *threo*- $\beta$ -hydroxy- $\alpha$ -amino acids or their phosphonic acid analogues by acidic hydrolysis (Scheme 9.2). The reactions of  $\alpha$ -substituted isocyanoacetate esters give, after acidic hydrolysis,  $\alpha$ -alkylated  $\alpha$ -amino acids.<sup>7,8</sup> The oxazolines obtained from *N*-methoxy-*N*-methyl- $\alpha$ -isocyanocetamide ( $\alpha$ -isocyano Weinreb amide)<sup>23</sup> can be transformed to *N,O*-protected  $\beta$ -hydroxy- $\alpha$ -amino aldehydes and ketones in high yield (Scheme 9.3).



Scheme 9.1

**Table 9.1.** Gold(I)-catalysed enantioselective aldol reaction of activated isocyanides with aldehydes<sup>a</sup>

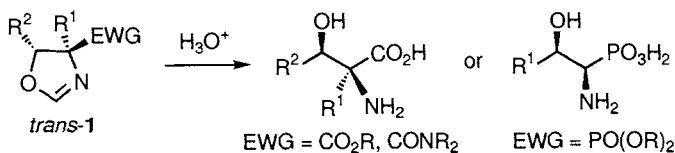
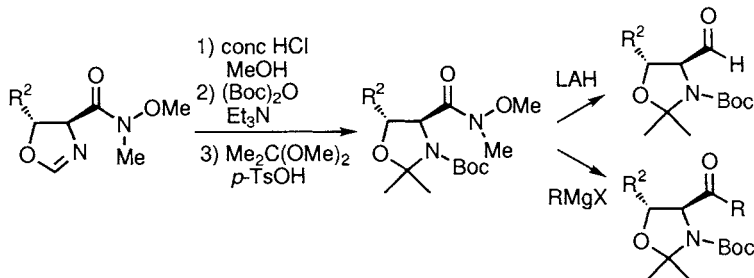
EWG	R <sup>1</sup>	R <sup>2</sup>	Ligand	<i>trans</i> : <i>cis</i>	ee (%) ( <i>trans</i> )
CO <sub>2</sub> Me	H	Ph	<b>2b</b>	89:11	93
CO <sub>2</sub> Me	H	Ph	<b>2c</b>	94:6	95
CO <sub>2</sub> Me	H	Me	<b>2a</b>	78:22	37
CO <sub>2</sub> Me	H	Me	<b>2d</b>	89:11	89
CO <sub>2</sub> Me	H	<i>i</i> -Pr	<b>2c</b>	99:1	94
CO <sub>2</sub> Me	H	<i>t</i> -Bu	<b>2d</b>	>99:1	97
CO <sub>2</sub> Me	H	( <i>E</i> )-PrCH=CH	<b>2d</b>	87:13	92
CO <sub>2</sub> Me	Me	Ph	<b>2d</b>	93:7	94
CO <sub>2</sub> Me	<i>i</i> -Pr	Ph	<b>2c</b>	54:46	92
CO <sub>2</sub> Me	<i>i</i> -Pr	H	<b>2c</b>	—	81
CONMe <sub>2</sub>	H	4-BnOC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub>	<b>2c</b>	>95:5	95
CON(Me)OMe	H	( <i>E</i> )-BnOCH <sub>2</sub> CH=CH	<b>2d</b>	96:4	95
PO(OPh) <sub>2</sub>	H	Ph	<b>2c</b>	>98:2	96

<sup>a</sup> Yield is generally high.

The terminal amino group of the chiral ligand is essential for the catalyst activity and the stereoselectivities.<sup>3</sup> Structure of the terminal amino group has a substantial effect on the stereoselectivity, six-membered ring amino groups such as piperidino or morpholino groups being generally efficient.<sup>3,4,16</sup> The

**Table 9.2.** Silver(I)-catalysed enantioselective aldol reaction of activated isocyanides with aldehydes<sup>a</sup>

EWG	R <sup>1</sup>	R <sup>2</sup>	Ligand	<i>trans:cis</i>	ee (%) ( <i>trans</i> )
CO <sub>2</sub> Me <sup>b</sup>	H	Ph	<b>2c</b>	96:4	80
CO <sub>2</sub> Me <sup>b</sup>	H	<i>i</i> -Pr	<b>2c</b>	99:1	90
SO <sub>2</sub> ( <i>p</i> -Tol) <sup>c</sup>	H	( <i>E</i> )-MeCH=CH	<b>2c</b>	97:3	85

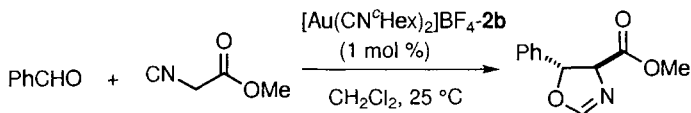
<sup>a</sup> Yield is generally high.<sup>b</sup> Reaction with 2 mol % of AgClO<sub>4</sub>·2 under slow addition conditions.<sup>c</sup> Reaction with 1 mol % of AgOTf·2.**Scheme 9.2****Scheme 9.3**

high efficiency of the gold catalysts has been explained by a transition state model as in structure **A**.<sup>15,27</sup> The chiral ligand chelates to the gold atom with the two phosphorus atoms leaving the two nitrogen atoms unco-ordinated. The  $\alpha$ -methylene protons of isocyanoacetate are activated through the coordination of the isocyano group to the gold atom, and the terminal amino group abstracts one of the activated  $\alpha$ -protons, forming an ion pair between enolate anion and ammonium cation. The attractive ligand-substrate interaction permits a favourable arrangement of the enolate and aldehyde on the gold atom in the stereodifferentiating transition state.

## Protocol 1.

### Enantioselective aldol reaction of methyl isocyanoacetate with benzaldehyde catalysed by a chiral diamino bisphosphine-gold (I) complex<sup>3</sup> (Scheme 9.4).

**Caution!** Carry out all procedures in a well-ventilated hood, and wear disposable vinyl or latex gloves and chemical-resistant safety goggles.



Scheme 9.4

### Equipment

- Magnetic stirrer
- Teflon-coated magnetic stirring bar (octagon 15 × 6.5 mm)
- Schlenk flask (30 mL)
- Syringes
- Thermostat
- Vacuum/inert gas source (argon)
- Water bath
- Kugelrohr distillation apparatus

### Materials

- Bis(cyclohexyl isocyanide)gold(I) tetrafluoroborate,<sup>28</sup> 25.1 mg, 0.050 mmol air-sensitive
- (*R*)-*N*-Methyl-*N*-[2-(diethylamino)ethyl]-1-[(*S*)-1',2-bis(diphenylphosphino)ferrocenyl]ethylamine,<sup>5</sup> 35.5 mg, 0.050 mmol
- Methyl isocyanoacetate,<sup>a</sup> 0.495 g, 5.00 mmol stench, irritant, corrosive, lachrymator
- Benzaldehyde,<sup>a</sup> 0.586 g, 5.50 mmol highly toxic, cancer suspect agent
- Dry, distilled dichloromethane, 5 mL toxic, irritant
- Dichloromethane for the transfer of a reaction mixture, 5 mL toxic, irritant

1. Place bis(cyclohexyl isocyanide)gold(I) tetrafluoroborate (25.1 mg, 0.050 mmol) and (*R*)-*N*-methyl-*N*-[2-(diethylamino)ethyl]-1-[(*S*)-1',2-bis(diphenylphosphino)ferrocenyl]ethylamine (35.5 mg, 0.050 mmol) in a 30 mL Schlenk flask with a magnetic stirring bar.
2. Purge the flask with argon.
3. Add dry distilled dichloromethane (5 mL) and stir the mixture at room temperature for 5 min.
4. Add methyl isocyanoacetate (0.495 g, 5.00 mmol) and immerse the flask into a water bath controlled at 25°C with a thermostat.
5. Add benzaldehyde (0.586 g, 5.50 mmol) and stir the mixture for 20 h. The completion of reaction can be checked by TLC (silica gel, hexane–ethyl acetate, 2:1).

6. Remove the solvent under reduced pressure.
7. Distil the residual liquid with a Khugelrohr (ca. 100°C, 1 mmHg) to obtain 1.05 g (98%) of the oxazoline or **3a** as a mixture of *trans*-(4*S*,5*R*) (93% ee) and *cis*-(4*R*,5*R*) (49% ee) isomers in a ratio of 89:11 (<sup>1</sup>H NMR).
8. Determine the enantiomeric excesses of both isomers by <sup>1</sup>H NMR analysis with a chiral shift reagent Eu(hfc)<sub>3</sub><sup>b</sup> or by GLC analysis with a chiral stationary phase capillary column (Sumichiral OA-520<sup>c</sup>).
9. The *trans*- and *cis*-isomers can readily be separated by flash column chromatography on silica gel (hexane–ethyl acetate, 5:1).<sup>d</sup>

<sup>a</sup> Purify by distillation before use.

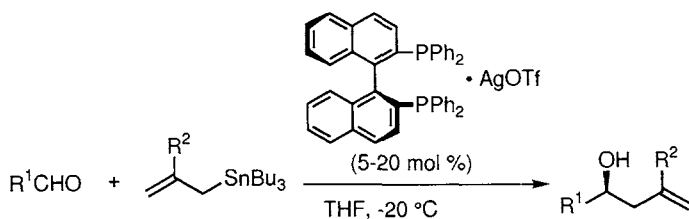
<sup>b</sup> Commercially available.

<sup>c</sup> Sumitomo Chemical Co. (Japan).

<sup>d</sup> Pre-dry the solvent over CaCl<sub>2</sub> and use the supernatant.

### 3. Enantioselective aldehyde allylation with allyltin reagents catalysed by a silver(I)–phosphine complex

The cationic silver(I)-BINAP complex is an efficient catalyst for the enantioselective allylation of aldehydes with allyltin reagents (Scheme 9.5).<sup>29</sup> The catalyst is prepared *in situ* from silver(I) triflate and the BINAP ligand in THF, and typically the reaction is carried out in the same solvent at –20°C. High enantioselectivity is observed with various aldehydes including aromatic, α,β-unsaturated, and saturated aliphatic aldehydes, whereas the scope for the saturated aliphatic aldehydes are somewhat limited (Table 9.3).



**Scheme 9.5**

Mechanistic studies suggest that the silver(I)-BINAP complex acts as a Lewis acid catalyst rather than an allylsilver reagent.

**Table 9.3.** Enantioselective allylation of aldehydes with allyltin reagents catalysed by a silver(I) complex of (*S*)-BINAP<sup>a</sup>

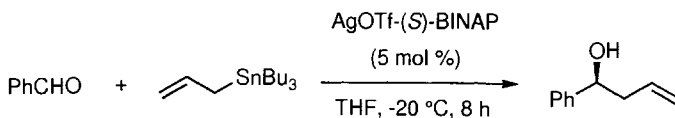
R <sup>1</sup>	R <sup>2</sup>	S/C <sup>b</sup>	Yield (%)	ee (%)
Ph	H	20	88	96 ( <i>S</i> )
Ph	Me	20	75	92 ( <i>R</i> ) <sup>c</sup>
2-MeC <sub>6</sub> H <sub>4</sub>	H	20	85	97
4-MeC <sub>6</sub> H <sub>4</sub>	H	20	59	97
( <i>E</i> )-PhCH=CH	H	6.7	83	88 ( <i>S</i> )
PhCH <sub>2</sub> CH <sub>2</sub>	H	5 <sup>d</sup>	47	88

<sup>a</sup> Allyltin reagent:aldehyde, 1–4:1.<sup>b</sup> Aldehyde:catalyst.<sup>c</sup> Reaction with (*R*)-BINAP.<sup>d</sup> The reaction was started with 0.1 equiv of the catalyst, and 0.1 equiv of the catalyst was added after 4 h.

## Protocol 2.

### Asymmetric allylation of benzaldehyde with allyltributyltin catalysed by (*S*)-BINAP·AgOTf Complex. Preparation of (*S*)-1-Phenyl-3-butene-1-ol<sup>29</sup> (Scheme 9.6)

**Caution!** Carry out all procedures in a well-ventilated hood, and wear disposable vinyl or latex gloves and chemical-resistant safety goggles.

**Scheme 9.6**

## Equipment

- Magnetic stirrer
- Syringes
- Vacuum/inert gas source (argon)
- Schlenk flask (20 mL)
- Syringe pump
- Cooling bath with dry ice–*o*-xylene

## Materials

- Silver trifluoromethanesulfonate,<sup>a</sup> 26.4 mg, 0.103 mmol irritant, light-sensitive
- (*S*)-(–)-2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl,<sup>a</sup> 66.5 mg, 0.107 mmol
- Benzaldehyde,<sup>b</sup> 208.0 mg, 1.96 mmol highly toxic, cancer suspect agent
- Allyltributyltin,<sup>b</sup> 663.1 mg, 2.00 mmol irritant
- Dry tetrahydrofuran (THF),<sup>c</sup> 6 mL flammable, irritant
- 1 M HCl solution in water, 10 mL toxic, corrosive
- Potassium fluoride, 1 g toxic, corrosive
- Magnesium sulfate hygroscopic

1. Ensure that all glass equipment has been dried in an oven before use.
2. Place silver trifluoromethanesulfonate (26.4 mg, 0.103 mmol) and (S)-(-)-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (66.5 mg, 0.107 mmol) in a 20 mL Schlenk flask with a magnetic stirring bar under argon atmosphere and exclusion of direct light. Add dry tetrahydrofuran (3 mL) and stir the mixture at 20°C for 10 min.
3. After cooling the resulting solution to -20°C, add benzaldehyde (208.0 mg, 1.96 mmol) dropwise. Then add a THF solution (3 mL) of allyltributyltin (663.1 mg, 2.00 mmol) over a period of 4 h with a syringe pump at -20°C.
4. After stirring for 4 h at this temperature, treat the reaction mixture with a mixture of 1 M HCl (10 mL) and solid KF (1 g) at ambient temperature for 30 min.
5. Filter off the resulting precipitate, dry the filtrate over MgSO<sub>4</sub> and concentrate *in vacuo*.
6. Purify the crude product by flash column chromatography on silica gel [hexane-ethyl acetate (10:1)] to give the (S)-enriched product (258 mg, 88% yield, 96% ee) as a colourless oil which displays the appropriate <sup>1</sup>H NMR (in CDCl<sub>3</sub>) and IR (neat).
7. Determine the enantiomeric excess by HPLC analysis (Daicel Chiralcel OD-H, hexane-*i*-PrOH, 20:1; flow rate, 0.5 mL/min), *t<sub>R</sub>* = 18.2 min (*R*-isomer), *T<sub>R</sub>* = 19.9 min (*S*-isomer).

<sup>a</sup> Commercially available products can be used without purification. Do not use aged ones.

<sup>b</sup> Purify benzaldehyde and allyltributyltin by distillation before use.

<sup>c</sup> Commercially available anhydrous THF (Aldrich) can be used as received.

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