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Copper(II) Triflate–Mediated Addition Reaction of α-Oxygenated Alkylsilanes to Imines for the Synthesis of Vicinal-Amino Alcohols

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Abstract: In the presence of copper(II) triflate, the addition reaction of α-oxygenated alkylsilanes to several imines proceeded smoothly to give the corresponding vicinal-amino alcohols in moderate yields.

Keywords: Addition reaction, copper(II) triflate, imine, α-oxygenated alkylsilane, vicinal-amino alcohol

Vicinal-amino alcohols and their derivatives have received considerable attention because of their versatility as synthetic intermediates in organic synthesis.[1] We have been interested in the development of new methods for the synthesis of nitrogen-containing compounds from the reaction between organometallic compounds and imines[2–6] and recently reported the addition reaction of α-oxygenated alkylstannanes to imines leading to vicinal-amino alcohol derivatives [Eq. (1)].[5] The reaction was effectively mediated by $Cu(OTf)_2$ to afford the addition products in good yields. Here, if less toxic α-oxygenated alkylsilanes react with imines instead of the stannanes, the reaction becomes an environmentally benign process. In addition, our interest in the comparison of reactivity between the silanes and the stannanes led us to investigate the reaction. We report herein a new

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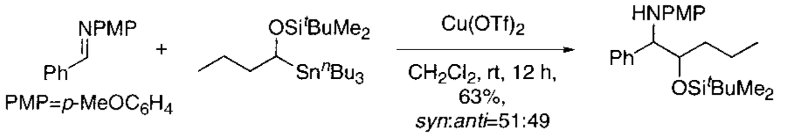
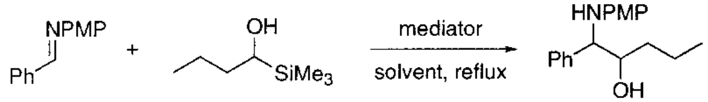
addition reaction of α-oxygenated alkylsilanes to imines mediated by $Cu(OTf)_2$, leading to vicinal-amino alcohols.



(1)

We initially examined the reaction of **1a** with **2a**[7,8] under various conditions to optimize the reaction conditions (Table 1). (These α-oxygenated alkylsilanes were prepared by modifications of the literature procedures for the analogous silanes.) As shown in entry 1, the reaction did not take place at all, and **1a** and **2a** remained unchanged under similar conditions applied in Eq. (1), suggesting that silane **1a** is less reactive than the corresponding stannane.[5] To overcome the low reactivity of **1a**, the reaction was carried out under reflux in CH_2Cl_2 (entry 2). Although the desired product **3a** was obtained in 42% yield with minimal diastereoselectivity, the reaction was still sluggish (entry 2). Fortunately, the rate of the reaction could be greatly accelerated by refluxing at higher temperature using 1,2-dichloroethane as a solvent while maintaining moderate yield (entry 3). Next, we examined the effect of mediators and found that $Cu(OTf)_2$ was the most

Table 1. Effect of mediators and solvents in the reaction of **1a** with **2a**[a]



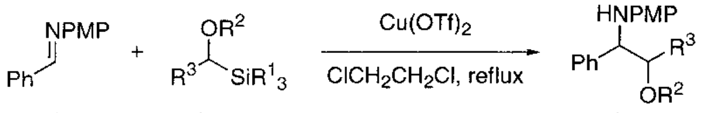
2a **1a** **3a**

Entry	Solvent	Mediator	Time (h)	Yield (%)	*Syn:anti*
1[b]	CH_2Cl_2	$Cu(OTf)_2$	24	0	—
2	CH_2Cl_2	$Cu(OTf)_2$	20	42	54:46
3	$ClCH_2CH_2Cl$	$Cu(OTf)_2$	3	46	49:51
4	$ClCH_2CH_2Cl$	$Sc(OTf)_3$	6	0	—
5	$ClCH_2CH_2Cl$	AgOTf	6	0	—
6	$ClCH_2CH_2Cl$	$BF_3 \cdot OEt_2$	6	0	—
7	$ClCH_2CH_2Cl$	Me_3SiOTf	6	0	—
8	$ClCH_2CH_2Cl$	$Sn(OTf)_2$	6	0	—
9	Benzene	$Cu(OTf)_2$	1.5	32	57:43
10	Toluene	$Cu(OTf)_2$	2	28	54:46
11	Tetrahydrofuran	$Cu(OTf)_2$	6	7	47:53
12	CH_3CN	$Cu(OTf)_2$	6	0	—

[a] Molar ratio **1a**–**2a**–mediator,1.0:1.0:1.0.

[b] The reaction was performed at room temperature.

Table 2. Effect of substituents in **1**[a]

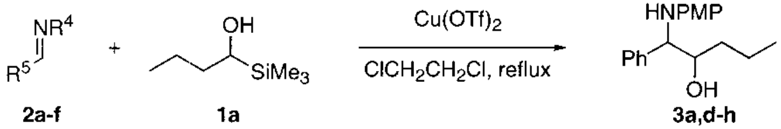


2a **1a-g** **3a-c**

	1					**3**		
Entry	SiR^1_3	R^2	R^3	Compound	Time (h)	Compound	Yield (%)	*Syn:anti*
1	$SiMe_3$	H	^{n}Pr	**1a**	3	**3a**	46	49:51
2	Si^tBuMe_2	H	^{n}Pr	**1b**	3	**3a**	46	42:58
3	$SiMe_2Ph$	H	^{n}Pr	**1c**	5	**3a**	39	57:43
4	$SiMe_3$	$SiMe_3$	^{n}Pr	**1d**	4	**3a**	32	47:53
5	$SiMe_3$	Si^tBuMe_2	^{n}Pr	**1e**	6	**3a**	39	57:43
6	$SiMe_3$	H	^{i}Pr	**1f**	5	**3b**	21	54:46
7	$SiMe_3$	H	Ph	**1g**	0.25	**3c**	0	—

[a] Molar ratio **1**–**2a**–$Cu(OTf)_2$, 1.0:1.0:1.0.

Table 3. Reactions of **1a** with imines **2**[a]



	2				**3**		
Entry	R^4	R^5	Compound	Time (h)	Compound	Yield (%)	*Syn:anti*
1	*p*-$MeOC_6H_4$	Ph	**2a**	3	**3a**	46	49:51
2	*p*-MeC_6H_4	Ph	**2b**	4	**3d**	48	51:49
3	*p*-ClC_6H_4	Ph	**2c**	3	**3e**	45	56:44
4	Ph	Ph	**2d**	4	**3f**	47	56:44
6	Ph	*p*-MeC_6H_4	**2e**	6	**3g**	45	61:39
7	Ph	*p*-ClC_6H_4	**2f**	4	**3h**	41	55:45

[a] Molar ratio **1a**–**2**–$Cu(OTf)_2$, 1.0:1.0:1.0.

promising among the mediators examined. The use of other mediators such as $Sc(OTf)_3$, AgOTf, $BF_3 \cdot OEt_2$, Me_3SiOTf, and $Sn(OTf)_2$ gave no product (entries 4–8). Finally, the optimized conditions were determined after surveying solvents (entries 3 and 9–12); 1,2-dichloroethane was the best solvent from the viewpoints of both the reaction rate and yield (entry 3).

We next performed the addition reaction of a series of silanes **1a–g**[7,8] with **2a** under the optimized reaction conditions to clarify the scope and limitation of the present reaction. The results are summarized in Table 2. Not only trimethylsilyl-substituted silane **1a** but both *t*-butyldimethylsilyl- and dimethylphenyl-substituted silanes, **1b** and **1c**, reacted with **2a** to give **3a** in moderate yields (entries 2 and 3). When *O*-silylated silanes **1d** and **1e** were used, **3a** was obtained instead of the corresponding *O*-silylated products (entries 4 and 5). Silane **1f**, which has an isopropyl group at the α-carbon, also underwent the addition reaction (entry 6), whereas a reaction using silane **1g** gave no product (entry 7).

The reactions of **1a** with several imines **2a–f** were carried out under the optimized conditions (Table 3). As can be seen from Table 3, **1a** smoothly reacted with aromatic imines to give the corresponding vicinal-amino alcohols in moderate yields.

In summary, we have developed a new addition reaction of α-oxygenated alkylsilanes to imines in the presence of $Cu(OTf)_2$. The present reaction provides a new method for the synthesis of vicinal-amino alcohols.

EXPERIMENTAL

General Procedure (Table 3, Entry 1)

To a mixture of **2a** (21 mg, 0.10 mmol) and $Cu(OTf)_2$ (36 mg, 0.10 mmol) in 1,2-dichloroethane (1.5 mL) was added **1a** (15 mg, 0.10 mmol) in 1,2-dichloroethane (0.5 mL) at room temperature. After being stirred for 3 h under reflux, the reaction was quenched with saturated aqueous $NaHCO_3$. After a usual workup, the crude product was purified by TLC (AcOEt–hexane 1/5) to give **3a** (13 mg, 46%, *syn:anti* = 49:51).

REFERENCES

1. Bergmeier, S. C. The synthesis of vicinal amino alcohols. *Tetrahedron* **2000**, *56*, 2561–2576.
2. Kagoshima, H.; Akiyama, T. Novel [3+2] cycloaddition reaction of alkenyl Fischer carbene complexes with imines leading to 3-pyrroline derivatives. *J. Am. Chem. Soc.* **2000**, *122*, 11741–11742.
3. Kagoshima, H.; Okamura, T.; Akiyama, T. The asymmetric [3+2] cycloaddition reaction of chiral alkenyl Fischer carbene complexes with imines: Synthesis of

optically pure 2,5-disubstituted-3-pyrrolidinones. *J. Am. Chem. Soc.* **2001**, *123*, 7182–7183.

4. Kagoshima, H.; Uzawa, T.; Akiyama, T. Catalytic, enantioselective propargyl- and allenylation reactions of α-imino ester. *Chem. Lett.* **2002**, 298–299.
5. Kagoshima, H.; Shimada, K. Copper(II) triflate–mediated addition reaction of α-oxygenated alkylstannanes to imines for the synthesis of vicinal-amino alcohol derivatives. *Chem. Lett.* **2003**, *32*, 514–515.
6. Kagoshima, H.; Takahashi, N. Copper(II) triflate–mediated addition reaction of α-sulfurated alkylstannanes to imines: Facile synthesis of vicinal-amino sulfides. *Chem. Lett.* **2004**, *33*, 962–963.
7. Linderman, R. J.; Ghannam, A. Synthesis of (α-hydroxyalky1)trialkylsilanes via reverse Brook rearrangement. *J. Org. Chem.* **1988**, *53*, 2878–2880.
8. Linderman, R. J.; Ghannam, A. Synthetic utility and mechanistic studies of the reverse Brook rearrangement. *J. Am. Chem. Soc.* **1990**, *112*, 2392–2398.