A Thiacalix[3]pyridine Copper(I) Complex as a Highly Active Catalyst for the Olefin Aziridination Reaction

Yuhei Tsukahara, Masakazu Hirotsu,* Shin-ichi Hattori, Yoshinosuke Usuki,* and Isamu Kinoshita
Department of Material Science, Graduate School of Science, Osaka City University, Sugimoto, Sumiyoshi-ku, Osaka 558-8585

A copper(I) complex with thiacalix[3]pyridine, [Cu-(Py$_3$S$_3$)]$_2$(PF$_6$)$_2$, is a competent catalyst for aziridination of olefins. The reaction of styrene (1 equiv) with PhI=NTs (1 equiv) at 20 °C produced *N*-(*p*-toluenesulfonyl)-2-phenyl-aziridine (71%, turnover number = 55) in the presence of 1.2 mol % catalyst under aerobic conditions. The turnover number increased up to 350 with a 0.12 mol % catalyst and a 5:1 styrene/PhI=NTs ratio in 41% yield.

Aziridines are useful synthetic intermediates in route to the nitrogen-containing compounds via nucleophilic ring-opening reactions under relatively mild conditions.[1] Nitrene transfer to olefins mediated by transition-metal complexes is one of the most straightforward synthetic strategies for the synthesis of aziridines.[1c,2] A wide variety of copper catalysts have been developed for the aziridination of olefins, and theoretical studies have been performed.[2c,3,4] The major problem to be solved is that most catalytic aziridinations require high catalyst loading and a large excess of olefin. Recently, several efficient aziridination reactions catalyzed by pyridine- or pyrazole-based copper complexes have been reported.[5] However, the pursuit of promising aziridination catalysts is still needed because the efficiency depends on the substrates and additional conditions.
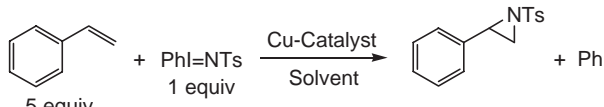
We have recently reported copper and rhodium complexes of a sulfur-bridged macrocyclic polypyridine ligand, thiacalix-[3]pyridine (Py$_3$S$_3$, Figure 1a).[6] The mononuclear rhodium(II) complex [Rh^{II}(Py$_3$S$_3$)$_2$]$^{2+}$ showed that the Py$_3$S$_3$ ligand tends to stabilize the lower oxidation states of a metal center.[6d] The dicopper(I) complex [Cu^I(Py$_3$S$_3$)]$_2$(PF$_6$)$_2$ (**1**) has a dimeric structure of Cu(Py$_3$S$_3$) units by compensatory coordination through the sulfur atoms as shown in Figure 1b.[6a] In solution, the dimeric [Cu(Py$_3$S$_3$)]$_2$$^{2+}$ readily dissociates in the presence of coordinating solvents (L) or ions (X$^-$), such as CH$_3$CN, Cl$^-$, Br$^-$, and I$^-$, accompanied by Cu–S bond cleavage and ligation of L or X$^-$ to the Cu atom to form monomeric [Cu(Py$_3$S$_3$)(L)]$^+$ or [Cu(Py$_3$S$_3$)(X)], respectively.[6a,6b] This implies that [Cu(Py$_3$S$_3$)]$_2$$^{2+}$ can act as a highly unsaturated copper(I) catalyst for a variety of organic reactions. Furthermore the monomeric species, also, are stable under air, and so the complex may be robust toward oxidative degradation in the

catalytic reaction. Here, we report an efficient aziridination of olefins catalyzed by the air-stable copper(I) complex **1**.

Aziridination reactions of styrene with [*N*-(*p*-toluenesulfonyl)imino]phenyliodinane (PhI=NTs)[7] were carried out using **1**, or halogen-coordinated complexes, [Cu(Py$_3$S$_3$)Cl] (**2**) and [Cu(Py$_3$S$_3$)I] (**3**).[6a,6b,8,9] We initially employed 5 equiv of styrene and 1 equiv of PhI=NTs (Table 1). In the use of 1 mol % of catalyst in acetonitrile (0.5 mol % for dimeric complex **1**), all the complexes catalyzed the aziridination to give *N*-(*p*-toluenesulfonyl)-2-phenylaziridine (**4**). The dimeric complex **1** (yield of **4**: 81%) was more efficient than the halogen-coordinated complexes (26% for **2**, 66% for **3**). In acetonitrile solutions, the dimeric and halogen-coordinated complexes would be converted to [Cu(Py$_3$S$_3$)(CH$_3$CN)]$^+$ by Cu–S and Cu–X (X = Cl and I) bond cleavage, respectively. The better yield of **4** by **1** is partly attributable to the poorer coordinating property of the sulfide S atoms in **1** than the halogeno ligand in **2** or **3**.

Under aerobic conditions, the reactions were almost identical to those under an argon atmosphere. This is an important advantage to the practical application considering that recently developed copper catalysts, which are highly active for aziridination, require an inert atmosphere and anhydrous conditions.[5] The resistance to oxidative degradation is consistent with the fact that **1** is stable to aerobic oxidation in solution. The turnover number (TON) of the aziridination reactions was markedly improved by changing 0.5 mol % catalyst loading (79%, TON = 160) to 0.1 mol % (41%, TON = 350), even though

Table 1. Aziridination of styrene with Py$_3$S$_3$–Cu^I catalysts

Catalyst /mol %	Solvent	T/°C, Time/h	Yield of **4**/%[c]	TON
1 (0.50)[a]	CH$_3$CN	r.t., 1	81	160
2 (1.0)[a]	CH$_3$CN	r.t., 1	26	28
3 (1.0)[b]	CH$_3$CN	r.t., 1	66	59
1 (2.5)[b]	CH$_3$CN	r.t., 1	93	38
1 (0.50)[b]	CH$_3$CN	r.t., 1	79	160
1 (0.12)[b]	CH$_3$CN	r.t., 1	41	350
1 (0.50)[b]	CH$_2$Cl$_2$	r.t., 1	94	195
1 (0.10)[b]	CH$_2$Cl$_2$	r.t., 1	19	195
1 (0.10)[b]	CH$_3$CN	0, 3	19	200
1 (0.10)[b]	CH$_3$CN	40, 1	44	390

[a]Reactions were carried out at room temperature under an argon atmosphere. [b]Reactions were carried out at room temperature under air. [c]Yields are given relative to PhI=NTs.

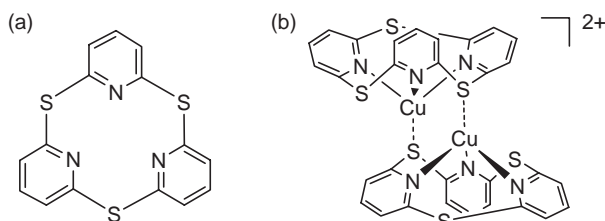**Figure 1.** Structures of (a) Py$_3$S$_3$ and (b) [Cu(Py$_3$S$_3$)]$_2$$^{2+}$.

Table 2. Aziridination of styrene catalyzed by **1** at a 1:1 reagent mole ratio

1/mol %	Yield of **4**/%[a]	TON
0.12	13	95
0.61	42	73
1.2	71	55
1.8	75	41
6.1	82	14

[a]Yields are given relative to PhI=NTs.

the yield decreased. Higher catalyst loading (2.5 mol %) of **1** led to high yield aziridination (93%), as shown in other catalyst systems.[2a–2c,3b–3d,5b] In dichloromethane, the reactions with **1** provided **4** in yields similar to those in acetonitrile. Reaction temperature little affected the yield of **4** in the 0.1 mol % catalyst loading.

Aliphatic alkenes, cyclooctene and 1-octene, were also aziridinated with 2.5 mol % **1** to produce the corresponding aziridines, **5** and **6**, in 85 and 40% yields, respectively. The highest catalytic activity of aziridination toward cyclooctene has been shown with the copper complexes of [2.1.1](2,6)-pyridinophane (1 mol % catalyst, 98% yield for cyclooctene).[5b] In these systems, the facial coordination of the ligands could make facile access of reactants to the remaining site possible.

It has been pointed out that the molar ratio of olefins and PhI=NTs appears to be crucial for improving the yield of aziridine: the excess of styrene was required.[2a,3b,5b] In our system, the reaction with an equimolar amount of styrene gave a 71% yield of the corresponding aziridine by using 1 mol % catalyst. As summarized in Table 2, the yield of aziridines increased as the amount of **1** increased. On the other hand, TON decreased with increasing the amount of **1**. These results suggest that the optimal conditions are largely affected by the amount of catalyst.

An electron-withdrawing COOR group attached to the C=C bond deactivates the substrate and generally causes a significant decrease in yield for aziridination reactions. We investigated the aziridinations of methyl acrylate, methyl cinnamate, and ethyl 2-methylacrylate using **1** as a catalyst (Table 3). The reactions of unsaturated esters (5 equiv) with PhI=NTs afforded the aziridination products **7–9** in moderate yields. An electron-donating group at the α position improves the yield for ethyl 2-methylacrylate ($R^1 = H$, $R^2 = Me$, and $R^3 = Et$), which is

higher than that for methyl acrylate ($R^1 = H$, $R^2 = H$, and $R^3 = Me$).

In summary, we have demonstrated that the thiacalix[3]-pyridine dicopper(I) complex **1** shows high catalytic activities for aziridination of various olefins. The compensatory coordination dimer **1** readily provides the mononuclear species with a largely open site in solution, retaining the copper(I) oxidation state. Since the reactions are performed under aerobic conditions without the removal of additional ligands, **1** is easy to handle and would be useful in practical synthetic processes.

References and Notes
1 a) J. B. Sweeney, *Chem. Soc. Rev.* **2002**, *31*, 247. b) I. D. G. Watson, L. Yu, A. K. Yudin, *Acc. Chem. Res.* **2006**, *39*, 194. c) P. Müller, C. Fruit, *Chem. Rev.* **2003**, *103*, 2905.
2 a) D. A. Evans, M. M. Faul, M. T. Bilodeau, *J. Org. Chem.* **1991**, *56*, 6744. b) Z. Li, K. R. Conser, E. N. Jacobsen, *J. Am. Chem. Soc.* **1993**, *115*, 5326. c) D. A. Evans, M. M. Faul, M. T. Bilodeau, B. A. Anderson, D. M. Barnes, *J. Am. Chem. Soc.* **1993**, *115*, 5328. d) H. Nishikori, T. Katsuki, *Tetrahedron Lett.* **1996**, *37*, 9245. e) M. J. Södergren, D. A. Alonso, P. G. Andersson, *Tetrahedron: Asymmetry* **1997**, *8*, 3563. f) P. Dauban, R. H. Dodd, *Tetrahedron Lett.* **1998**, *39*, 5739. g) Y. Usuki, Y. Fukuda, H. Iio, *ITE Lett. Batteries, New Technol. Med.* **2001**, *2*, 237; CAN 136:184068.
3 a) P. J. Pérez, M. Brookhart, J. L. Templeton, *Organometallics* **1993**, *12*, 261. b) D. A. Evans, M. M. Faul, M. T. Bilodeau, *J. Am. Chem. Soc.* **1994**, *116*, 2742. c) K. M. Gillespie, C. J. Sanders, P. O'Shaughnessy, I. Westmoreland, C. P. Thickitt, P. Scott, *J. Org. Chem.* **2002**, *67*, 3450. d) H. Suga, A. Kakehi, S. Ito, T. Ibata, T. Fudo, Y. Watanabe, Y. Kinoshita, *Bull. Chem. Soc. Jpn.* **2003**, *76*, 189. e) R. R. Conry, A. A. Tipton, W. S. Striejewske, E. Erkizia, M. A. Malwitz, A. Caffaratti, J. A. Natkin, *Organometallics* **2004**, *23*, 5210. f) W. Sun, E. Herdtweck, F. E. Kühn, *New J. Chem.* **2005**, *29*, 1577. g) X. Wang, K. Ding, *Chem.—Eur. J.* **2006**, *12*, 4568. h) H. Martínez-García, D. Morales, J. Pérez, D. J. Coady, C. W. Bielawski, D. E. Gross, L. Cuesta, M. Marquez, J. L. Sessler, *Organometallics* **2007**, *26*, 6511.
4 P. Brandt, M. J. Södergren, P. G. Andersson, P.-O. Norrby, *J. Am. Chem. Soc.* **2000**, *122*, 8013.
5 a) H. V. R. Dias, H.-L. Lu, H.-J. Kim, S. A. Polach, T. K. H. H. Goh, R. G. Browning, C. J. Lovely, *Organometallics* **2002**, *21*, 1466. b) A. N. Vedernikov, K. G. Caulton, *Org. Lett.* **2003**, *5*, 2591. c) M. A. Mairena, M. M. Díaz-Requejo, T. R. Belderraín, M. C. Nicasio, S. Trofimenko, P. J. Pérez, *Organometallics* **2004**, *23*, 253. d) F. Mohr, S. A. Binfield, J. C. Fettinger, A. N. Vedernikov, *J. Org. Chem.* **2005**, *70*, 4833.
6 a) R. Tanaka, T. Yano, T. Nishioka, R. Nakajo, B. K. Breedlove, K. Kimura, I. Kinoshita, K. Isobe, *Chem. Commun.* **2002**, 1686. b) I. Kinoshita, A. Hamazawa, T. Nishioka, H. Adachi, H. Suzuki, Y. Miyazaki, A. Tsuboyama, S. Okada, M. Hoshino, *Chem. Phys. Lett.* **2003**, *371*, 451. c) T. Nishioka, Y. Onishi, K. Nakajo, J. Guo-Xin, R. Tanaka, I. Kinoshita, *Dalton Trans.* **2005**, 2130. d) R. T. Hamazawa, T. Nishioka, I. Kinoshita, T. Takui, R. Santo, A. Ichimura, *Dalton Trans.* **2006**, 1374.
7 Y. Yamada, T. Yamamoto, M. Okawara, *Chem. Lett.* **1975**, 361.
8 General procedure of aziridination reaction: To a solution of a copper complex were added olefins (1–5 equiv) and PhI=NTs (1 equiv). The mixture was stirred for 1 h at room temperature. The yield of the corresponding aziridine was determined by ^{1}H NMR using triphenylmethane as an internal standard. The ^{1}H NMR spectra of the aziridine products were identical to the reported data in the literature.
9 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.

Table 3. Aziridination of unsaturated esters catalyzed by **1**

R^1, R^2, R^3	Product	Yield/%[a]	TON
H, H, Me	**7**	33	13
Ph, H, Me	**8**	54	21
H, Me, Et	**9**	67	26

[a]Yields are given relative to PhI=NTs.