Syntheses of acetonitrile ligated copper complexes with perfluoroalkoxy aluminate as counter anion and their catalytic application for olefin aziridination

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ABSTRACT

Acetonitrile ligated copper complexes with perfluoroalkoxy aluminate $Al\{OC(CF_3)_3\}_4^-$ as weakly coordinating counter anion are successfully synthesized. Aziridination of various olefins with PhINTs catalyzed by copper(II) complex $[Cu(II)(NCCH_3)_6][Al\{OC(CF_3)_3\}_4]_2$ affords good to excellent yields (up to 96%) and very high turnover frequency (higher than 5000 h^{-1}) under mild conditions.

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Aziridination of olefins is a very important transformation, since aziridines are valuable synthetic intermediates for a wide range of nitrogen-containing compounds[1–3] and are often present as substructures in natural products, exhibiting various biological properties, such as antitumor and antibiotic activities.[4] However, the catalytic aziridination of olefins had drawn little attentions before 1991, when a copper catalyst system for this reaction was reported by Evans.[5] Since then, various transition metal complexes such as those of rhodium,[6–8] copper,[9–16] ruthenium,[17,18] cobalt,[19] iron,[20,21] manganese,[22] nickel,[23] silver,[24] and gold[25] have been shown to catalyze the transformation. The efficient systems usually contain 2–10 mol % of a soluble catalyst and nitrene sources, for example *N*-tosyliminophenyliodinane (PhINTs) and bromamine-T.[15]

Weakly coordinating counter anions (WCAs) have been applied extensively in catalysis during the last decade, due to the fact that WCAs have an effect of stabilizing the cations and rendering the intermediate species more accessible to substrate coordination. The applications of WCAs include polymerization reactions[26–28] as well as various organic transformations.[29,30,19] Yet, so far there is only one report[15] which shows WCAs having a significant positive effect on catalytic olefin aziridination. However, the reported catalysts, which apply $B\{C_6H_3(m-CF_3)_2\}_4^-$ as counter anion, were generated in situ and no characterization data were available. Hence, a more detailed exploration of the effect of WCAs on catalytic aziridination would be most helpful and necessary.

Very recently, a simple and cost efficient procedure to synthesize $[Ag(NCCH_3)_4][Al\{OC(CF_3)_3\}_4]$ was reported.[31] Herein, we describe the syntheses of copper complexes (Fig. 1) $[Cu(NCCH_3)_4][Al\{OC(CF_3)_3\}_4]$ (**1**) and $[Cu(NCCH_3)_6][Al\{OC(CF_3)_3\}_4]_2$(**2**), as well as first results of their applications in catalytic olefin aziridination.

Complexes **1** and **2** were prepared from CuCl and CuCl$_2$, respectively, using the silver salt $[Ag(NCCH_3)_4][Al\{OC(CF_3)_3\}_4]$ in a metathesis reaction with good yields, as shown in Scheme 1.

Complexes **1** and **2** were characterized by IR spectroscopy, elemental analysis, and ^{1}H NMR. The IR shifts of v(CN) absorption are observed at 2268 cm^{-1} and 2305 cm^{-1} (**1**), and 2293 cm^{-1} and 2332 cm^{-1} (**2**). For ^{1}H NMR, the chemical shift of the acetonitrile protons of complex **2** (δ = 1.96 ppm) is more close to that of free acetonitrile (δ = 1.83 ppm) than complex **1** (δ = 2.14 ppm). The results of elemental analysis also match the expectations adequately.

The complexes were examined for their catalytic activity for olefin aziridination (Scheme 2), with PhINTs as nitrene source and styrene as substrate. As indicated in Table 1, only a moderate yield was obtained with compound **1** (entry 1), yet an excellent yield was achieved when compound **2** was applied (entry 2). The yield remained excellent (90%) when only 0.1 mol % of **2** was applied (entry 3), however, at the expense of a prolonged reaction time. Nevertheless, with the same catalyst loading, the obtained yield is still the best known to date for a copper-catalyzed styrene aziridination. It is assumed that the robust WCA $Al\{OC(CF_3)_3\}_4^-$,[32] which stabilizes the Cu(II) cation and provides higher accessibility

* Corresponding author. Tel.: +49 (0)89 289 13096; fax: +49 (0)89 289 13473.
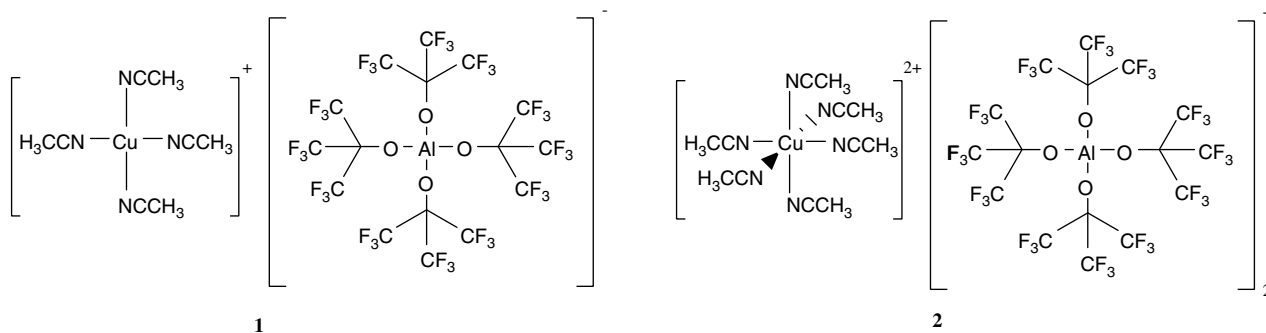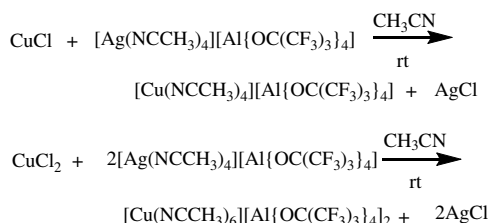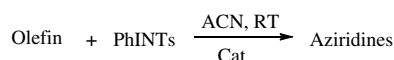*E-mail address:* fritz.kuehn@ch.tum.de (F. E. Kühn).

Figure 1. Acetonitrile ligated copper complexes **1** and **2**.

$$CuCl + [Ag(NCCH_3)_4][Al\{OC(CF_3)_3\}_4] \xrightarrow[rt]{CH_3CN}$$

$$[Cu(NCCH_3)_4][Al\{OC(CF_3)_3\}_4] + AgCl$$

$$CuCl_2 + 2[Ag(NCCH_3)_4][Al\{OC(CF_3)_3\}_4] \xrightarrow[rt]{CH_3CN}$$

$$[Cu(NCCH_3)_6][Al\{OC(CF_3)_3\}_4]_2 + 2AgCl$$

Scheme 1. Syntheses of **1** and **2**.

$$Olefin + PhINTs \xrightarrow[Cat.]{ACN, RT} Aziridines$$

Scheme 2. Catalytic olefin aziridination.

Table 1
Aziridination of styrene by copper complexes[a]

No.	Catalyst	Loading (mol %)	Time	Yield[b] (%)
1	**1**	0.5	20 min	63
2	**2**	0.5	3 min	91
3	**2**	0.1	6 h	90
4[c]	**2**	0.5	24 h	54
5[c]	**2**	1.0	20 min	68
6	CuCl$_2$	0.5	10 min	31
7	Cu(BF$_4$)$_2$	0.5	5 min	47
8	Cu(ClO$_4$)$_2$	0.5	5 min	33
9[d,f]	[Cu(NCCH$_3$)$_6$][**1**]$_2$	0.5	5 min	61
10[e,f]	[Cu(NCCH$_3$)$_6$][**2**]$_2$	0.5	5 min	59

[a] Styrene (2.5 mmol), PhINTs (0.5 mmol), mesitylene (20 μl) and the catalyst were stirred in 2.0 ml acetonitrile at room temperature.
[b] GC yield.
[c] 0.5 mmol styrene.
[d] **1** = B(C$_6$F$_5$)$_4$.
[e] **2** = B{C$_6$H$_3$(m-CF$_3$)$_2$}$_4$.
[f] For the syntheses and application of the two complexes, see Ref. 33.

of the cation to substrate coordination, is responsible for the extraordinary high catalytic activity of **2**. In all reactions, trace amounts of p-toluene sulfonamide are detected as by-product by GC. To further explore the catalytic activity of **2**, a 1:1 ratio of styrene and PhINTs was applied (entry 4). As expected, the reaction goes to completeness with prolonged time but produces a higher amount of by-product. Yet when a higher catalyst loading (entry 5) is applied, the reaction time decreases strongly from 24 h to 20 min. In both reactions (entries 4 and 5), much more p-toluene sulfonamide is detected. The result is in accord with Evans' earlier report,[5] in which considerable p-toluene sulfonamide was ob-
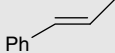
tained. This is described as being due to decomposition of PhINTs in the presence of copper-based catalysts, when long reaction times are necessary to complete the reaction.
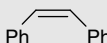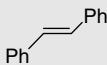
Copper(II) chloride (entry 6) and copper salts with traditional WCAs (entries 7 and 8) were also applied as catalysts under the same conditions, however, only low yields were obtained. When the counter anions were changed to the widely used B(C$_6$F$_5$)$_4^-$ and [B{C$_6$H$_3$(m-CF$_3$)$_2$}$_4$]$_2^-$ (entries 9 and 10), the yields were higher, but still significantly lower than the yields obtained with **2**.

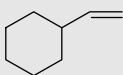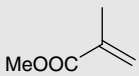The substrate scope was then further explored, as indicated in Table 2. Under the standard conditions (2 ml MeCN, 1–3 mol % catalyst, 1 equiv of PhINTs, 5 equiv of olefin, 25 °C), the reactions proceed in good to excellent yields with both aromatic and aliphatic olefins. With styrene as substrate, it is noteworthy that the turnover frequency (TOF) is as high as 5000 h^{-1}, which is—to the best of our knowledge—the highest for a copper-catalyzed aziridination reported in the literature to date (entry 1). With methyl-substituted styrenes, complex **2** affords the corresponding aziridines in excellent yields similar to that of the styrene reaction (entries 2–4). Remarkably, the stereochemistry of both trans- and cis-β-methylstyrene remains in the respective products. The results are consistent with Evans' earlier investigation, in which a Cu(ClO$_4$)$_2$ system was applied,[34] and a concerted mechanism[35,34] was suggested. On the other hand, contrasting results[36,25,20] reported by other groups suggested a stepwise mechanism for gold, iron, and even for copper systems, for example, CuBr$_2$ and Cu(acac)$_2$,[34] indicating the reaction mechanism of catalytic aziridination is both metal and counter anion dependent. Sterically hindered cis/trans-stilbene was also tested (entries 5 and 6). With cis-stilbene (entry 5) excellent yield was obtained, but only moderate stereospecificity was achieved. This observation is due to the higher stability of the trans isomer of the product. On the other hand, aziridination of trans-stilbene (entry 6) leads to pure trans product. The relatively low yield and longer reaction time is probably due to the applied solvent (mixture of acetonitrile and dichloromethane), since trans-stilbene is a solid which is barely soluble in acetonitrile. Simple cyclic olefins were also shown to be suitable substrates (entries 7 and 8). As expected, cis-cyclooctene, possessing a weaker and more reactive C=C bond, is more reactive than cyclohexene. However, higher catalyst loadings and longer reaction times are necessary for the less active vinylcyclohexane and 1-octene to obtain satisfactory yields (entries 9 and 11). Nevertheless, the results are still comparable or superior to the best literature values. Good to excellent yields were obtained for less sterically hindered aliphatic olefins (entries 10, 12, and 13), including the electron deficient substrate methyl methacrylate (entry 12).

The WCA Al{OC(CF$_3$)$_3$}$_4^-$ was successfully incorporated into copper complexes **1** and **2** by straightforward metathesis reaction of CuCl/CuCl$_2$ and [Ag(NCCH$_3$)$_4$][Al{OC(CF$_3$)$_3$}$_4$]. A preliminary investigation of their catalytic potentials shows that complex **2** is

Table 2
Aziridination of olefins with PhINTs catalyzed by **2**

No.	Substrate	L. (mol %)	t	Prod.	Yield[a] (%)
1	Ph⎯ (styrene)	1.0	<1 min	**1a**	93[b]
2	Ph⎯ (cis)	1.0	5 min	**1b**	95 cis:trans = 96:4[c]
3	Ph⎯ (trans)	1.0	5 min	**1c**	90 cis:trans = 1:99[c]
4	Ph (α-methylstyrene)	1.0	3 min	**1d**	91
5	Ph⎯Ph (stilbene)	1.0	3 min	**1e**	94 cis:trans = 2:1[c]
6[d]	Ph, Ph	1.0	40 min	**1f**	80[e]
7	(cyclooctene)	1.0	5 min	**1g**	85[b]
8	(cyclohexene)	1.0	20 min	**1h**	80
9	(vinylcyclohexane)	1.0 3.0	8 h 30 min	**1i**	25 85
10	(2,3-dimethyl-2-butene)	1.0	40 min	**1j**	86
11	1-Octene	1.0 2.0	16 h 1.5 h	**1k**	45 60
12	MeOOC	1.0	20 min	**1l**	96
13	(norbornene)	1.0	10 min	**1m**	95

[a] Isolated yield.
[b] Yield determined by GC.
[c] The ratio of cis and trans isomers was detected by ^{1}H NMR.
[d] A solvent mixture of acetonitrile (1 ml) and DCM (2.5 ml) is applied as the reaction media.
[e] cis Isomer is not detected by ^{1}H NMR.

a very efficient catalyst for olefin aziridination. Its main advantages include low catalyst loading, high yields, very high turnover numbers, short reaction times, high stereospecificity, a wide substrates range and mild reaction conditions. However, the low solubility of **2** limits its application to solvents such as dichloromethane and toluene. Examinations such as modifying the counter anion and the ligands are currently going on in our laboratories, to lead to a better solubility and possibly of even higher catalytic activity.

Supplementary data

Experimental procedures and spectral data for all compounds. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.07.162.

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