A Cationic Diruthenium Amidinate, $[(\eta^5\text{-}C_5Me_5)Ru(\mu_2\text{-}i\text{-}PrN{=}C(Me)Ni\text{-}Pr)Ru(\eta^5\text{-}C_5Me_5)]^+$, as an Efficient Catalyst for the Atom-Transfer Radical Reactions

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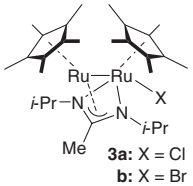
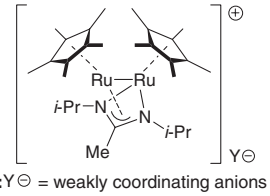
A cationic diruthenium amidinate, $[(\eta^5\text{-}C_5Me_5)Ru(\mu_2\text{-}i\text{-}PrN{=}C(Me)Ni\text{-}Pr)Ru(\eta^5\text{-}C_5Me_5)]^+$, is generated by treatment of $(\eta^5\text{-}C_5Me_5)Ru(\mu_2\text{-}i\text{-}PrN{=}C(Me)Ni\text{-}Pr)Ru(Cl)(\eta^5\text{-}C_5Me_5)$ (**3a**) with $NaPF_6$ or other metal salts of weakly coordinating anions, which is active towards catalytic atom transfer radical cyclization of *N*-allyl trichloroacetamides and related reactions.

Atom-transfer radical reaction has now become one of the most important carbon–carbon bond-forming reactions which is utilized for synthetic organic chemistry and polymer synthesis.[1] Since our initial discovery of the atom-transfer radical cyclization (ATRC) of allyl trichloroacetates and *N*-allyltrichloroacetamides,[2a] transition metal-catalyzed ATRC has been developed for a unique method of carbo- and heterocycles, and efficient catalysts have been a research target. Among several transition metal complexes so far reported,[1,3] a 1:1 mixture of CuCl and bipyridine is the most powerful catalyst system for cyclization of *N*-protected *N*-allyltrichloroacetamides to the corresponding α,α,γ-trichlorinated γ-lactams.[2,3] As new catalysts showing comparable reactivity to the CuCl/bipyridine system, we have recently reported mononuclear ruthenium amidinates, $(\eta^5\text{-}C_5Me_5)Ru(amidinate)$ (**1**) and $(\eta^5\text{-}C_5Me_5)Ru(amidinate)Cl$ (**2**), to be novel catalysts for the cyclization of *N*-allyltrichloroacetamides.[3c] It is important that these new catalysts are particularly efficient for cyclization of a precursor of pyrrolidizine alkaloids such as trachelantamidine and pseudoheliotridane, the activity of which is much higher than that with the CuCl/bipyridine system. The coordinatively unsaturated nature of the ruthenium amidinates leads to this high catalytic activity; however, it also imposes a drawback in that the ruthenium amidinates are sensitive to air and moisture and difficult to handle. In this paper, we wish to report a solution to this synthetic demerit: the finding that a coordinatively unsaturated species generated in situ from a stable diruthenium amidinate **3a** behaves as a powerful catalyst for the cyclization of *N*-allyltrichloroacetamides and its related reactions.

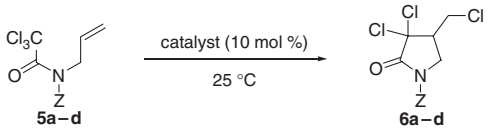


3a: X = Cl
b: X = Br



4: $Y^{\ominus}$ = weakly coordinating anions

As reported previously, isolable coordinatively unsaturated diruthenium complexes **4** were synthesized by anion exchange of stable diruthenium amidinates **3**.[4b] The isolated **4** $[Y{=}B(C_6F_5)_4]$ was found to be active towards the cyclization of *N*-allyl-*N*-benzyltrichloroacetamide **5a**; the reaction proceeded smoothly to afford **6a** in 94% yield within 30 min (Table 1, Entry 2). Since reversible generation of cationic species was deduced from solution dynamics of **3a** in CH_2Cl_2,[4b] a solution of **3a** exhibited some catalytic activity towards cyclization of **5a** and **5b** (Entries 1 and 7). Addition of sodium salts of weakly coordinating anions facilitated the generation of **4**. In fact, cyclization of **5a** or its *N*-tosyl homologue **5b** by catalysis of a 1:1 molar ratio of **3a** and $NaPF_6$ or $NaBPh_4$ was complete at room temperature within 30 min to give the corresponding product in quantitative yields (Entries 3, 4, 8, and 9). Catalytic activity of these cationic catalysts is higher than that using the mononuclear complexes **1** and **2**, particularly for the cyclization of **5b** (Entries 5, 6, 10, and 11). At 1 mol % loading, this catalyst system afforded **5b** in 92% yield (Entry 12). Application of this new catalyst system to the cyclization of other *N*-allyltrichloroacetamides is summarized in Table 1.



5a–d **6a–d**

Table 1. Radical cyclization of *N*-allyltrichloroacetamides **5a–d**

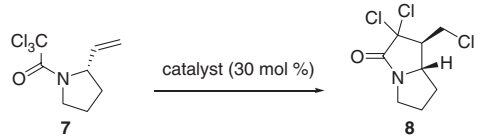
Entry	Substrate	Catalyst	Solvent	Time /h	Yield /%
1	**5a** (Z = Bn)	**3a**	CH_2Cl_2	4	30
2	**5a**	**4** $[Y{=}B(C_6F_5)_4]$	CH_2Cl_2	0.5	94
3	**5a**	**3a** + $NaPF_6$	CH_2Cl_2	0.5	>99
4	**5a**	**3a** + $NaBPh_4$	CH_2Cl_2	0.5	>99
5	**5a**	**1**	toluene	4	85
6	**5a**	**2**	toluene	4	88
7	**5b** (Z = Ts)	**3a**	CH_2Cl_2	4	97
8	**5b**	**3a** + $NaPF_6$	CH_2Cl_2	0.5	>99
9	**5b**	**3a** + $NaBPh_4$	CH_2Cl_2	0.5	>99
10	**5b**	**1**	benzene	4	31
11	**5b**	**2**	benzene	4	0
12[a]	**5b**	**3a** + $NaBPh_4$	CH_2Cl_2	3	92
13	**5c** (Z = Ph)	**3a** + $NaPF_6$	CH_2Cl_2	1	52
14[b]	**5d** (Z = Allyl)	**3a** + $NaPF_6$	CH_2Cl_2	1	>99

[a] 1 mol % of catalyst was used. [b] 2.5 mol % of catalyst was used.

The efficiency of **3a** with the aid of $NaPF_6$ or $NaBPh_4$ as the catalyst eventually led to three important aspects in the γ-lactam synthesis by ATRC. First, the pyrrolidizine alkaloid precursor mentioned above was obtained in high yield by this catalyst system (Table 2, Entry 1). It is noteworthy that the catalyst efficiency in this particular substrate is much higher than that with the CuCl/bipyridine system, and comparable to that with **1** or **2**, which are known to be one of the most powerful catalysts for this type of reaction.

Second, high catalytic activity of the in situ-generated cationic diruthenium amidinate was also demonstrated in the cyclization of a *N*-allyldichloroacetamide **9**, which is known as a less reactive substrate than the trichlorinated homologue. In fact, with the conventional CuCl/bipy system, it is necessary to apply high reaction temperatures (>80 °C) or to load large amounts of the catalyst (≈30 mol %) to obtain the product in good yields.[5]

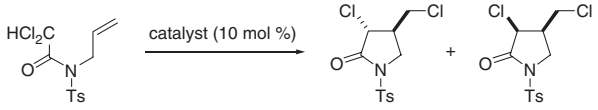
Although the neutral complex **3a** was not very effective for the cyclization of **9** (12 h, 25% yield), the cationic diruthenium species prepared in situ from **3a** and $NaBPh_4$ (10 mol % each) gave the product **10** in 88% yield, when the reaction was performed at 25 °C for 3 h (Table 3, Entries 1 vs 2). The observed diastereoselectivity (*trans*/*cis* = 7.0:1) of the reaction with cationic diruthenium amidinate was controlled kinetically.[6]



7 **8**

Table 2. Radical cyclization of the cyclic trichloroacetamide **7**

Entry	Catalyst	Solvent	Conditions	Yield /%
1	**3a** + $NaPF_6$	CH_2Cl_2	rt, 3 h	90
2	**1**	benzene	rt, 13 h	90
3	**2**	benzene	rt, 3 h	85
4	CuCl / Bipy	$ClCH_2CH_2Cl$	80 °C, 2 h	97



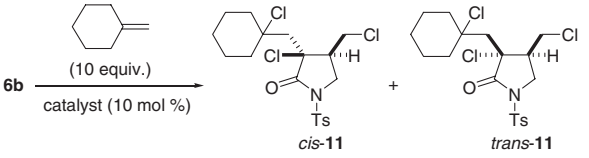
9 *trans*-**10** *cis*-**10**

Table 3. Radical cyclization of the *N*-allyldichloroacetamide **9**

Entry	Catalyst	Solvent	Conditions	Yield /%	*trans*/*cis*[a]
1	**3a**	CH_2Cl_2	25 °C, 12 h	25	6.9:1
2	**3a** + $NaBPh_4$	CH_2Cl_2	25 °C, 3 h	88	7.0:1
3	CuCl / Bipy	CH_2Cl_2	25 °C, 3 h	24	7.4:1
4	CuCl / Bipy	$ClCH_2CH_2Cl$	80 °C, 1 h	95	4.0:1

[a] Determined by ^1H NMR.

Third, the cationic diruthenium catalytic species is useful for activation of an α-chlorine atom of the γ-lactam **6b** followed by intermolecular addition reaction to alkenes. (Table 4). Although high reaction temperatures are required for the carbon–carbon bond forming reaction at the α-position of the 2-pyrroridinone **6b** catalyzed by the CuCl/bipy system,[6b] the reaction of **6b** (0.2 mmol) with 10 equiv. of methylenecyclohexane in the presence of in situ-generated cationic species (10 mol %) proceeded even at 25 °C (Entry 1). The diastereomer ratio of the adducts **11** was kinetically controlled (5.7:1); this is in contrast to the fact that the product ratio obtained by the CuCl/bipy catalyst system at 83 °C was thermodynamically controlled (>99:1) (Entry 3).[6b]



cis-**11** *trans*-**11**

Table 4. Reaction of the lactam **6b** with methylenecyclohexane

Entry	Catalyst	Solvent	Conditions	Yield /%	*cis*/*trans*[a]
1	**3a** + $NaBPh_4$	CH_2Cl_2	25 °C, 10 h	57	5.7:1
2	CuCl / Bipy	CH_2Cl_2	25 °C, 12 h	<5	-
3	CuCl / Bipy	$ClCH_2CH_2Cl$	83 °C, 1 h	>99	>99:1

[a] Determined by ^1H NMR.

In summary, we have discovered a new catalyst species, $[(\eta^5\text{-}C_5Me_5)Ru(\mu_2\text{-}i\text{-}PrN{=}C(Me)N i\text{-}Pr)Ru(\eta^5\text{-}C_5Me_5)]^+$, which is useful for metal-catalyzed ATRC to access γ-lactams and its related reaction.[7] The catalytic activity is often comparable to the conventional CuCl/bipy catalyst, and even higher in extreme cases: synthesis of the pyrrolidizine alkaloid skeleton, cyclization of a *N*-allyl dichloroactetamide, and the activation of an α-chlorine atom of the dichlorinated lactam, as described above. Since the catalyst species can be generated in situ from air- and moisture stable **3a** simply by treatment with $NaPF_6$ or $NaBPh_4$, there is no problem in handling air- and moisture sensitive orgamometallics like **1** and **2**. We believe that this catalyst system can be widely applicable to metal-catalyzed radical reactions, and further studies are now in progress.

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6 It is known that equilibrium between the *trans*- and *cis*-isomers of this type of compounds easily took place in the presence of transition metal complexes over 80 °C, and the thermodynamically controlled ratio of *trans*- to *cis*-**10** reached ca. 4:1: a) G. A. Slough, *Tetrahedron Lett.*, **34**, 6825 (1993). b) S. Iwamatsu, H. Kondo, K. Matsubara, and H. Nagashima, *Tetrahedron*, **55**, 1687 (1999).

7 A typical experimental procedure: a trichloroacetamide **5b** (0.2 mmol), **3a** (0.02 mmol), and $NaBPh_4$ (0.02 mmol) were dissolved in freshly distilled, carefully degassed dichloromethane (1.5 mL) under an argon atmosphere. After the solution was stirred at 25 °C for 30 min, the product **6b** was obtained by silica gel chromatography (CH_2Cl_2 as an eluent) in quantitative yield (Table 1, Entry 9).

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