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Organoruthenium(II) and (III) amidinates, (η^5-C_5Me_5)Ru(η-amidinate) and (η^5-C_5Me_5)RuCl(η-amidinate), as unique redox catalysts for the intramolecular Kharasch reactions: Facile access to a pyrrolizidine alkaloid skeleton under mild conditions†

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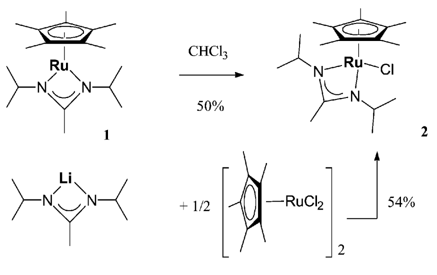
A novel organoruthenium(III) amidinate, (η^5-C_5Me_5)RuCl(η-^{i}PrN=C(Me)N^{i}Pr) (2), has been prepared by oxidation of organoruthenium amidinate, (η^5-C_5Me_5)Ru(η-^{i}PrN=C(Me)N^{i}Pr) (1), by organic chlorides; both 1 and 2 are found to be good catalysts for atom-transfer cyclization of N-allyltrichloroacetamides which are useful for successful preparation of a pyrrolizidine alkaloid skeleton under mild conditions.

It is widely accepted that coordinatively unsaturated transition metal species are often involved in catalytic transformation of organic molecules.[1] We have recently discovered unique ruthenium(II) amidinates which formally have 16 valence electrons and show high reactivity towards various two electron donor ligands.[2] In the course of our studies on the redox properties of these ruthenium amidinates, we were aware that (η^5-C_5Me_5)Ru(η-amidinate) showed two one-electron oxidation waves which were assignable to Ru(II)/Ru(III) and Ru(III)/Ru(IV) oxidation processes in the cyclic voltammetry.[3] This implies the possibility of chemical transformation of organic molecules on (η^5-C_5Me_5)Ru(η-amidinate) by way of Ru(II)/Ru(III), Ru(III)/Ru(IV), or Ru(II)/Ru(IV) redox processes, which may lead to the discovery of novel catalysis of organoruthenium amidinates. The oxidative addition of allylic substrates involving change of the oxidation state of the ruthenium center from Ru(II) to Ru(IV) is actually accomplished by the reaction of (η^5-C_5Me_5)Ru(η-amidinate) with allylic substrates, forming cationic Ru(IV)-η^3-allyl complexes;[4] this leads to the finding that (η^5-C_5Me_5)Ru(η-amidinate) acts as a catalyst for nucleophilic substitution reactions of allyl carbonates.[4] Discovery of the catalytic reaction involving the Ru(II)/Ru(IV) redox process prompted us to consider the possibility of catalytic reaction through Ru(II)/Ru(III) or Ru(III)/Ru(IV) processes. We wish to report here the reaction of (η^5-C_5Me_5)Ru(η-^{i}PrN = C(Me)N^{i}Pr) (**1**) with certain organic chlorides which forms a novel ruthenium (III) amidinate **2**. Furthermore, both **1** and **2** are active towards atom-transfer cyclization of N-allyltrichloroacetamides, which is a typical catalytic reaction involving the one-electron redox process of transition metal species. Of particular interest is application of these catalysts to synthesis of a pyrrolizidine alkaloid skeleton, which proceeds under much milder conditions than the conventional catalyst systems composed of copper.[5,6]

As reported earlier, the reaction of **1** with allylic halides resulted in formation of a Ru–C bond to give organoruthenium(IV) amidinates, [(η^5-C_5Me_5)Ru(η^2-amidinate)(η^3-allyl)]$^+$X$^-$. In sharp contrast, treatment of **1** with chloroform afforded green paramagnetic microcrystals, of which mass spectrum and elemental analysis suggested the product to be a novel organoruthenium(III) amidinate, (η^5-C_5Me_5)RuCl(η^2-^{i}PrN=C(Me)N^{i}Pr) (**2**) (50% yield) (Scheme 1). The same paramagnetic molecule was alternatively synthesized by the reaction of [(η^5-C_5Me_5)RuCl$_2$]$_2$ with lithium amidinate in 54% yield as shown in Scheme 1. The structure of **2** was unequivocally determined by crystallography, and its ORTEP drawing is illustrated in Fig. 1.‡ The arrangement of the center of the C_5Me_5 ligand, two nitrogen atoms, and the chlorine atom is pseudo tetrahedral, and the Ru–C (C_5Me_5) and Ru–N bond distances are similar to those seen in the crystal structures of [(η^5-C_5Me_5)Ru(η^2-amidinate)(η^3-allyl)]$^+$X$^-$. Other organic halides such as benzyl chloride, CCl_4, and CH_2Cl_2, were also reactive with **1** to form **2**. Despite potential formation of (η^5-C_5Me_5)RuCl$_2$(η^2-^{i}PrN=C(Me)N^{i}Pr) by prolonged treatment of **1** or **2** with chloroform or other organic halides, no diamagnetic product due to the Ru(IV) amidinate species was observed.§

It is well known that abstraction of a chlorine atom from CCl_4, $CHCl_3$, and other polyhalogenated compounds by transition metal salts or complexes is an important elementary



Scheme 1 Preparation of the Ru(III)-amidinate **2**.

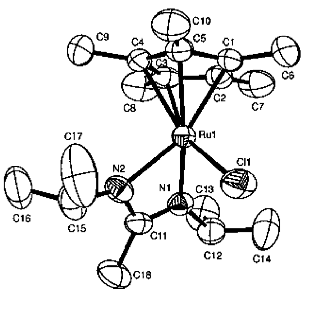


Fig. 1 ORTEP drawing of **2** showing 50% thermal ellipsoids. Selected bond lengths (Å) and angles (°); Ru(1)–N(1) 2.096(4), Ru(1)–N(2) 2.088(4), Ru(1)–Cl(1) 2.3896(14), Ru(1)–C(1–5)$_{av}$ 2.2066(5), C(11)–N(1) 1.305(7), C(11)–N(2) 1.316(7), C–C(ring)$_{av}$ 1.4228(7), Cl(1)–Ru(1)–C(Cp* centroid) 125.9(2), N(1)–Ru(1)–C(Cp* centroid) 134.1(2), N(2)–Ru(1)–C(Cp* centroid) 131.8(2).

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† Electronic supplementary information (ESI) available: representative experimental details and crystallographic data. See http://www.rsc.org/suppdata/cc/b2/b209369c/

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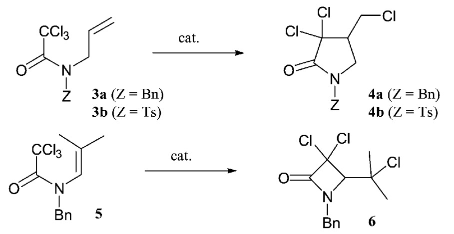
step in catalytic addition of polyhalogenated compounds to olefins (the Kharasch reaction), of which the intramolecular version has received considerable attention from organic chemists as a unique method for construction of carbo- or heterocycles.[5] As reported previously, we discovered CuCl-(bipy) to be one of the most powerful catalysts for the intramolecular Kharasch reaction of N-allyltrichloroacetamides, in particular for cyclization of the substrates having electron-withdrawing N-substituents.[6] Despite the versatile utility of CuCl(bipy) for the cyclization of N-allyltrichloroacetamides, application of the copper catalyst to the cyclization of certain N-alkyl-N-allyltrichloroacetamides sometimes gives unsatisfactory results.[6,7] We have found the catalytic activity of the ruthenium amidinates, **1** and **2**, in the cyclization of N-allyl or N-vinyltrichloroacetamides as shown in Scheme 2 and Table 1. Although they were not efficient for the cyclization of a N-tosyl derivative **3b**, comparable catalytic activity to CuCl(bipy) was seen in the reaction of N-alkyl derivatives **3a** and **5**. Further investigation provided a dramatic advantage of the ruthenium-amidinate catalysts in the cyclization of a vinyl pyrrolidine derivative **7** (Scheme 3, Table 2) to a bicyclic lactam **8**, which is a precursor of pyrrolizidine alkaloids, trachelanthamidine and pseudoheliotriadane.[7] Access to **8** from **7** was reported by Seijas and coworkers in 1992 using a stoichiometric amount of CuCl in CH_3CN at 160 °C.[7] Our efforts to perform the reaction at lower temperatures by using CuCl(bipy) catalyst attained partial success; the cyclization proceeded at 80 °C. To our surprise, use of **1** and **2** as the catalyst resulted in smooth cyclization of **7** to **8** even at room temperature.

In summary, one electron oxidation of coordinatively unsaturated ruthenium amidinate **1** is accomplished by chlorine-atom abstraction from chloroform to form the novel Ru(III) amidinate **2**, which is the first organoruthenium(III) amidinate isolated and characterized. Both **1** and **2** exhibit catalytic activity towards atom transfer cyclization of N-allyl or N-vinyl trichloroacetamides, being extremely efficient for the cyclization of a particular N-allyltrichloroacetamide **7**, which is a precursor of pyrrolizidine alkaloid skeletons.¶ These results demonstrate potential utility of **1** and **2** as molecular catalysts in organic synthesis, and further exploration of other catalytic reactions of **1** or **2** involving the one or two electron redox process is underway.

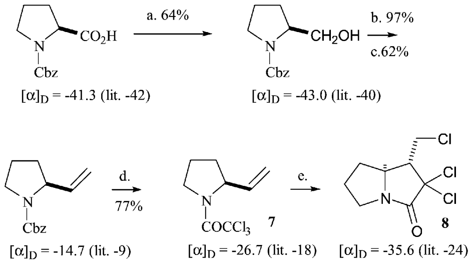


Scheme 2 Cyclization of N-allyl and N-vinyltrichloroacetamides.

Table 1 Cyclization of **3a**, **3b**, and **5** by copper or ruthenium catalysts

Substrate	Catalyst (mol%)	Solvent	Product	Time/h	Yield (%)
3a	CuCl(bipy) (10)	CH_2Cl_2	**4a**	1	99
3a	**1** (10)	toluene	**4a**	4	85
3a	**2** (10)	toluene	**4a**	4	88
3b	CuCl(bipy)	CH_2Cl_2	**4b**	1	99
3b	**1** (10)	toluene	**4b**	4	31
3b	**2** (10)	toluene	**4b**	4	0
5	CuCl(bipy) (10)	CH_2Cl_2	**6**	1	85
5	**1**(10)	toluene	**6**	4	35
5	**2** (10)	toluene	**6**	4	82

All reactions were carried out at room temperature under an argon atmosphere. Catalyst turnover numbers were generally 3–15.



a. Et_3N, $ClCO_2Et$, $NaBH_4$ in THF at r.t.; b. $(ClCO)_2$, DMSO, Et_3N in CH_2Cl at -60°C; c. $RhCl(PPh_3)_3$ (5 mol%), PPh_3, iPrOH, $TMSCHN_2$ in THF at r.t.; d. HBr/AcOH r.t. then CCl_3COCl, DMAP in CH_2Cl_2 at r.t.; e. see Table II

Scheme 3

Table 2 Cyclization of the cyclic trichloroacetamide **7**

Catalyst (mol%)	Solvent	Temp/°C	Time/h	Yield (%)	Ref.
CuCl (95)	MeCN	160	2	93	7
CuCl(bipy) (30)	CH_2Cl_2	80	2	87	
1 (30)	benzene	r.t	12	90	
2 (30)	benzene	r.t	3	85	

All reactions were carried out under an argon atmosphere.

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Notes and references

‡ *Crystal data* for $C_{18}H_{32}ClN_2Ru$ **2**, M = 412.98, monoclinic, a = 13.149(2), b = 9.255(3), c = 16.412(3) Å, V = 1997.2(8) Å^3, T = 293 K, space group $P2_1/n$, Z = 4, μ = 0.918 mm^{-1}, 4728 reflections measured, 4573 unique (R_{int} = 0.0509), wR_2 = 0.0924, wR_2 = 0.1159 (all data). CCDC 194483 and 194484. See http://www.rsc.org/suppdata/cc/b2/b209369c/ for crystallographic files in CIF or other electronic format.

§ Cyclic voltammograms of **1** and **2** suggested that both the Ru(II)/Ru(III) (*i.e.* between **1** and **2**) and the Ru(III)/Ru(IV) (*i.e.* between **2** and (η^5-C_5Me_5)$RuCl_2$(η^2-amidinate)) redox processes could take part in the catalytic cyclization mechanism.

¶ As shown in Scheme 3, modification of the synthetic procedure of **7** was made to avoid racemization at step c using the rhodium-catalyzed olefination of aldehydes by trimethylsilyldiazomethane, which was recently reported by Lebel and coworkers.[8] Enantiomeric purity as well as the stereochemistry between the angular proton and the chloromethyl group of **8** were unequivocally confirmed by crystallographic study (see ESI†).

1 For leading references, R. Poli, *Chem. Rev.*, 1996, **96**, 2153; K. G. Caulton, *New J. Chem.*, 1994, **18**, 25; R. H. Crabtree, *The Organometallic Chemistry of the Transition Metals*, Wiley, New York, 3rd edn., 2000.
2 Y. Yamaguchi and H. Nagashima, *Organometallics*, 2000, **19**, 725; T. Hayashida, Y. Yamaguchi, K. Kirchner and H. Nagashima, *Chem. Lett.*, 2001, 954; H. Kondo, Y. Yamaguchi and H. Nagashima, *J. Am. Chem. Soc.*, 2001, **123**, 500; H. Kondo, K. Matsubara and H. Nagashima, *J. Am. Chem. Soc.*, 2002, **124**, 534.
3 H. Kondo, Y. Yamaguchi and H. Nagashima, *Chem. Commun.*, 2000, 1075; H. Kondo, A. Kageyama, Y. Yamaguchi, M. Haga, K. Kirchner and H. Nagashima, *Bull. Chem. Soc. Jpn.*, 2001, **74**, 1927.
4 For reviews: B. M. Trost and D. L. Van Vranken, *Chem. Rev.*, 1996, **35**, 96. See also, Y. Morisaki, T. Kondo and T. Mitsudo, *Organometallics*, 1999, **18**, 4742, and references therein.
5 For a review, J. Iqbal, B. Bhatia and N. K. Nayyar, *Chem. Rev.*, 1994, **94**, 519.
6 H. Nagashima, N. Ozaki, M. Ishii, K. Seki, M. Washiyama and K. Itoh, *J. Org. Chem.*, 1993, **58**, 464. Recent progress, see; S. Iwamatsu, K. Matsubara and H. Nagashima, *J. Org. Chem.*, 1999, **64**, 9625; J. S. Bryans, N. E. A. Chessum, A. F. Parsons and F. Ghelfi, *Tetrahedron Lett.*, 2001, **42**, 2901.
7 J. A. Seijas, M. P. Vazquez-Tato, L. Castedo, R. J. Estevez, M. G. Onega and M. Ruiz, *Tetrahedron*, 1992, **48**, 1637.
8 H. Lebel, V. Paquet and C. Proulx, *Angew. Chem., Int. Ed.*, 2001, **40**, 2887.

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