Carbon radical addition–cyclization reaction induced by ruthenium-photocatalyst under visible light irradiation

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ABSTRACT

In the presence of $Ru(bpy)_3Cl_2 \cdot 6H_2O$ and $(i\text{-}Pr)_2NEt$, the photo-induced cascade radical addition–cyclization–trapping reaction proceeded in aqueous media. When $i\text{-}C_3F_7I$ was employed as a radical precursor, the iodine atom-transfer radical cyclization proceeded even in the absence of $(i\text{-}Pr)_2NEt$. Under the photo-induced conditions, ICH_2CN and ICH_2CF_3 also worked well as carbon radical precursors. The photo-induced reductive electron-transfer to CF_3SO_2Cl promoted the chlorine atom-transfer radical cyclization.

1. Introduction

The use of visible light-activated transition metal catalysts such as ruthenium[1] or iridium[2] complexes has attracted substantial attention because of environmental compatibility.[3] In recent years, these photocatalysts have been shown to induce the synthetically useful transformation via single-electron transfer redox process.[4] Some of these catalysts have the potential to induce the organic reactions in aqueous media.[5] However, less is known about the aqueous-medium carbon–carbon bond formation using photocatalysts.[5] Interestingly, both the reducing and oxidizing abilities of the excited state $[Ru(bpy)_3]^{2+}*$ in H_2O (-0.86 V and $+0.84$ V vs SCE, respectively) are slightly greater than those in CH_3CN (Fig. 1).[6] Additionally, its excited state has a comparatively long lifetime of 650 ns in H_2O as well as 890 ns in CH_3CN.[7] Therefore, our laboratory is more interested in developing the cascade construction of carbon–carbon bonds in aqueous media based on the ruthenium photocatalyst-induced radical reactions under visible light irradiation.

We recently reported the Et_3B-induced cascade reaction starting from the polarity-mismatched perfluoroalkyl radical addition.[8,9] In principle, the reactions of strictly neutral species such as uncharged
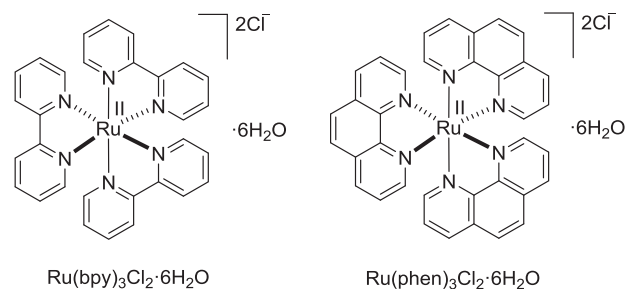
Redox potential in excited state of Ru(bpy)$_3$Cl$_2$·6H$_2$O in H$_2$O

Potential of $[Ru(bpy)_3]^{3+}/[Ru(bpy)_3]^{2+*}$ couple (-0.86 V vs. SCE)
Potential of $[Ru(bpy)_3]^{2+*}/[Ru(bpy)_3]^{+}$ couple ($+0.84$ V vs. SCE)
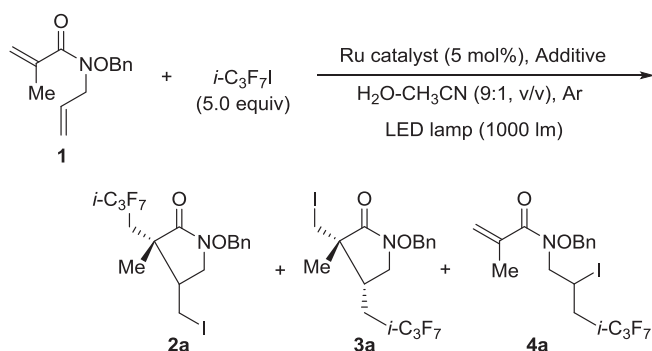
Fig. 1. Ruthenium photocatalysts.

free radicals are not affected by the presence of water.[10–12] Thus, we next investigated this cascade radical reaction in aqueous media by using a ruthenium catalyst under visible light irradiation.[13] In this paper, we report the detailed experiments to probe the utility of ruthenium catalysts in the aqueous-medium reaction with several carbon radical precursors and the viability of CF_3SO_2Cl in the chlorine atom-transfer radical cyclization reaction using ruthenium catalyst.

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2. Results and discussion

2.1. Cascade reaction starting from *i*-C₃F₇ radical addition

Our recent studies showed that Et₃B was an excellent radical initiator for the cascade reaction of substrate **1** starting from the polarity-mismatched perfluoroalkyl radical addition.[8,14,15] We firstly investigated the ruthenium-catalyzed radical addition–cyclization–trapping reaction of **1** in aqueous media (Scheme 1). In the presence of ruthenium catalyst, the biphasic solution of **1** and *i*-C₃F₇I (5 equiv) in H₂O/CH₃CN (9:1, v/v) was stirred with LED light irradiation under Ar atmosphere. As shown in Table 1, no reaction was observed in the absence of photocatalyst (entry 1). When Ru(bpy)₃Cl₂·6H₂O was employed as a water-soluble photocatalyst, the reaction proceeded to give the products **2a**, **3a**, and **4a**. In order to generate the ruthenium species having the reduction property, several amines were selected as the reductive quenchers (entries 2–5).[7,16] As expected, the generation of *i*-C₃F₇ radical from *i*-C₃F₇I was promoted in presence of 1,2,2,6,6-PMP (1,2,2,6,6-pentamethylpiperidine). After being stirred for 3 h, the products **2a**, **3a**, and **4a** were obtained in 67% combined yield (entry 2). The addition of PhNMe₂ could lead to enhancement in chemical yield and cis/trans diastereoselectivity of product **2a** (entry 3). In contrast, chemical yield decreased by using the bulky amine quencher Ph₃N having more positive oxidation potential (+0.86 V) (entry 4). Among the tested amines, (*i*-Pr)₂NEt having less positive oxidation potential (+0.68 V) promoted the reaction with good activity to form **2a**, **3a**, and **4a** in 77% combined yield (entry 5). A prolonged reaction led to the similar result (entry 6). Interestingly, when (*i*-Pr)₂NEt was employed, the acceptable yield was observed within 1 h (entry 7). In these biphasic reactions, the aqueous phase changed into dark red color indicating the red crystalline salt Ru(bpy)₃Cl₂·6H₂O was mainly solved in the aqueous phase. Under analogous reaction conditions, tris-(1,10-phenanthroline)ruthenium(II) chloride, Ru(phen)₃Cl₂·6H₂O, worked well (entry 8).

Next, the effect of solvent on chemical efficiency was studied (Table 2). The replacement of H₂O/CH₃CN with CH₃CN led to a slight decrease in chemical yield (entry 1). Decreasing the amount of *i*-C₃F₇I to 2 equiv led to a low chemical yield even after being stirred for 15 h (entry 2). The monophasic reaction in DMF took long reaction time and half of the starting material remained (entry 3). The similar trend was observed in protic solvent such as CH₃OH (entry 4). Interestingly, the formation of the uncyclized product **4a** was not observed in monophasic organic solvent (entries 1–4). In contrast, the biphasic aqueous-medium reactions proceeded smoothly to give good yields of the products **2a**–**4a** (entries 5–7). In the absence of organic co-solvent, the biphasic reaction in H₂O also proceeded effectively without any problem (entry 8). Next, the reaction on a 1.0 mmol scale of **1** was carried out in *i*-C₃F₇I (0.7 mL) in the absence of solvent (entry 9). However, the reaction did not proceed effectively to give the complex mixture. This result indicates that the use of H₂O led to an enhancement in chemical efficiency, because the catalyst Ru(bpy)₃Cl₂·6H₂O is not soluble in *i*-C₃F₇I. In our previous study using Et₃B as a radical initiator,[8] we reported that the perfluoroalkyl radicals predominantly added to an electron-deficient alkene moiety of **1**, though perfluoroalkyl radicals are classified into electrophilic radicals.[17,18] Similarly, the polarity-mismatched addition of perfluoroalkyl radicals was observed under the photocatalytic conditions to give the polarity-mismatched perfluoroalkylation product **2a** as a major product. Interestingly, the uncyclized product **4a** was newly formed under the present photocatalytic conditions, which was not obtained in the Et₃B-induced reaction in organic solvent.

Table 2
Effect of solvent for the ruthenium-catalyzed reaction

Entry	Solvent	Time (h)	Yield[a] (%)	Ratio[b] (2a/3a/4a)	dr of 2a[b] (cis/trans)
1	CH₃CN	3	58 (23)	66:34:Trace	77:23
2[c]	CH₃CN	15	43 (51)	66:34:Trace	76:24
3	DMF	15	39 (43)	66:34:Trace	76:24
4	CH₃OH	15	50 (31)	66:34:Trace	73:27
5	H₂O/CH₃OH (9:1, v/v)	3	70	62:22:16	79:21
6	H₂O/CH₂Cl₂ (9:1, v/v)	3	68 (15)	60:28:12	75:25
7	H₂O/toluene (9:1, v/v)	3	72	59:28:13	75:25
8	H₂O	3	75	62:23:15	77:23
9	None	15	Complex mixture		

[a] Combined yield. The yield in parentheses is for the recovered substrate **1**.
[b] Determined by ¹H NMR analysis.
[c] *i*-C₃F₇I of 2 equiv was employed.

Scheme 1. Ruthenium-catalyzed cascade radical addition-cyclization of **1**.

Table 1
Ruthenium-catalyzed reaction of **1** under visible light irradiation

Entry	Catalyst	Additive[a] (1.1 equiv)	Potential[b] (V vs SCE)	Time (h)	Yield[c] (%)	Ratio[d] (2a/3a/4a)	dr of 2a[d] (cis/trans)
1	None	None		15	NR		
2	Ru(bpy)₃Cl₂·6H₂O	1,2,2,6,6-PMP	+0.73	3	67	69:26:5	76:24
3	Ru(bpy)₃Cl₂·6H₂O	PhNMe₂	+0.81	3	71	63:23:14	89:11
4	Ru(bpy)₃Cl₂·6H₂O	Ph₃N	+0.86	3	28 (39)	64:15:21	80:20
5	Ru(bpy)₃Cl₂·6H₂O	(*i*-Pr)₂NEt	+0.68	3	77	64:24:12	76:24
6	Ru(bpy)₃Cl₂·6H₂O	(*i*-Pr)₂NEt		15	79	64:24:12	77:23
7	Ru(bpy)₃Cl₂·6H₂O	(*i*-Pr)₂NEt		1	66 (4)	63:24:13	83:17
8	Ru(phen)₃Cl₂·6H₂O	(*i*-Pr)₂NEt		3	71	65:25:10	73:27

[a] Amine of 1.1 equiv was added as the reductive quencher.
[b] Potential of amines in CH₃CN. See: Refs. 7 and 16.
[c] Combined yield. The yield in parentheses is for the recovered substrate **1**.
[d] Determined by ¹H NMR analysis.