Feature

Green Oxidation of Amines to Imines Based on the Development of Novel Catalytic Systems Using Molecular Oxygen or Hydrogen Peroxide

31

Kuniaki Marui^a Akihiro Nomoto^a Haruo Akashi^b Akiya Ogawa^{*a}

^a Department of Applied Chemistry, Graduate School of Engineering, Osaka Prefecture University, 1-1 Gakuen-cho, Nakaku, Sakai, Osaka 599-8531, Japan ogawa@chem.osakafu-u.ac.jp

^b Research Institute of Natural Sciences, Okayama University of Science, Ridai-cho, Okayama 700-0005, Japan akashi@rins.ous.ac.jp



Received: 10.10.2015 Accepted: 14.10.2015 Published online: 04.11.2015 DOI: 10.1055/s-0035-1560363; Art ID: ss-2015-z0593-fa

Abstract Amines are transformed into the corresponding imines by environmentally benign catalytic oxidation reactions. Gaseous oxygen or hydrogen peroxide is used as the oxidant, and water is the only byproduct. When a vanadium complex is used as the catalyst in an ionic liquid, the amine oxidation successfully proceeds with recycling of the catalyst. Amine oxidation with hydrogen peroxide as an oxidant in water is also attained by using copper(II) sulfate as catalyst. In addition, photoinduced oxidation of amines to imines is conducted by using oxygen as the oxidant in the presence of a zinc-chlorin complex as catalyst.

Key words green oxidation, imine synthesis, molecular oxygen, hydrogen peroxide, ionic liquid, water, photocatalysis

Oxidation is one of the most important and fundamental organic reactions, and about 30% of industrial processes involve oxidation reactions.¹ Nonetheless, stoichiometric or excess amounts of heavy metal oxidants, such as chromium(VI) oxide, explosive peroxides, and nitric acid are conventionally used as oxidants in industrial processes.² These oxidants pose serious risks to the environment and human safety; therefore, the development of eco-friendly oxidation methods using catalytic amounts of safe metal complexes is strongly desired.³ From the viewpoint of green chemistry, green oxidation reactions require the following characteristics: (1) the use of sustainable and inexpensive earth-abundant transition metals; (2) the use of molecular oxygen or hydrogen peroxide as the terminal oxidant, where water is the only byproduct; (3) the use of eco-friendly solvents such as water, ionic liquids, and fluorous solvents in place of flammable organic solvents; in particular, water is the most desirable solvent, due to its low cost, safety, and great abundance;⁴ and/or (4) the use of inexhaustible sunlight (visible light) and mild reaction conditions. However, examples of metal-complex-catalyzed oxidations with molecular oxygen (or H_2O_2) in water as the only solvent are still rare. Precious metals (e.g., Au, Ru, Pd), high-pressure oxygen or air, and stoichiometric amounts of bases are often required.⁵

Judging from the Clarke numbers (V: 0.015, Cu: 0.0055, Zn: 0.007, Pd: 1×10^{-6} , Ru: 5×10^{-7}), vanadium, copper, and zinc are relatively abundant elements. In addition, vanadium and copper have excellent oxidizing potentials [Zn(II)/Zn(0): -0.76 V; Cu(II)/Cu(I): 0.16 V; Fe(III)/Fe(II): 0.77 V; V(V)/V(IV): 0.96 V].

With these considerations in mind, we recently developed a novel system for the aerobic oxidation of benzylic alcohols to the corresponding aldehydes or ketones catalyzed by vanadium–bipyridyl complexes in water as the sole solvent (Equation 1).⁶



Equation 1 Oxidation of benzylic alcohols catalyzed by vanadiumbipyridyl complexes in water under oxygen or air (0.1 MPa)

Furthermore, we extended the developed reactions to the oxidation of amines to imines. Imines are very important for the synthesis of industrial materials, biologically active compounds (e.g., amides, chiral amines), nitrogencontaining heterocycles (e.g., oxazolidines), and other nitrogen-containing compounds (e.g., hydroxyamines and nitrones).⁷ Numerous methodologies have been developed to synthesize imines, including the oxidation of primary or secondary amines, the condensation of amines with aldehydes, and the oxidative condensation of amines with alco-

Feature

hols.⁸ In particular, extensive efforts have concentrated on developing efficient methods for the highly selective synthesis of imines from primary amines without the concomitant formation of other undesired nitrogen-containing compounds.⁹

In this article, we wish to report three novel eco-friendly oxidation reactions of amines to imines, by using new catalytic oxidation systems. The first is a vanadium-catalyzed green oxidation of amines to imines under a molecular oxygen atmosphere and by using an ionic liquid as an eco-friendly solvent. The vanadium catalyst can be efficiently recycled in this system. As the second process, we have developed a copper-catalyzed green oxidation of amines to imines with hydrogen peroxide in water under very mild reaction conditions (r.t., 1.5 h). The third system is a photoinduced (visible light-irradiated) oxidation of amines to imines under the atmosphere of molecular oxygen in benzotrifluoride (BTF) as an eco-friendly, organic/fluorous hybrid solvent¹⁰ in the presence of a zinc-chlorin complex. These eco-friendly oxidation reactions are useful for the synthesis of imines, and will further the development of green oxidation reactions in organic synthesis.

Biographical Sketches





Akihiro Nomoto was born in Osaka (Japan) in 1969 and earned his B.S. and Ph.D. degrees from Osaka University under the supervision of Professor Toshikazu Hirao. He held a post-

doctoral fellowship with Profes-

Kuniaki Marui was born in

Oita (Japan) in 1987. He gradu-

ated from Osaka Prefecture Uni-

versity in 2012 and obtained his

Haruo Akashi was born in Fukuoka (Japan) in 1963 and earned his B.S. and Ph.D. degrees from the Okayama University of Science under the supervision of Professor Takashi Shibahara. He held a postdoctoral fellowship with Professor sor Yoshiaki Kobuke at Nara Institute of Science and Technology, Professor Yoshito Tobe at Osaka University, and Professor Minoru Inaba at Doshisha University. He then joined Prof. Akiya Ogawa's group as an as-

master degree in synthetic or-

ganic chemistry at Osaka Pre-

fecture University under the di-

rection of Prof. Akiya Ogawa.

Kiyoshi Isobe at the Institute for Molecular Science, and he then became an assistant professor in 1991, lecturer in 1997, associate professor in 2003, and professor in 2008 at the Okayama University of Science. He also held a postdoctoral fellow-

Akiya Ogawa was born in Osaka (Japan) in 1957 and received his Ph.D. degree from Osaka University (1985) under the supervision of Professor Noboru Sonoda. He worked as postdoctoral researcher of the Japan Society for the Promotion of Science (1985–1987), as assistant professor at Osaka University (1987–1995, Professor Noboru Sonoda group), as associate professor at Osaka University (1995–2000, Professor Toshikazu Hirao group), and as visiting professor at the University of Pittsburgh (1996, Professor Dennis P. Curran group). In 2000, he joined the Department of Chemistry at Nara Since then, he has been a Ph.D. student focusing on the development of environmentally benign oxidation reactions.

sistant professor in 2005 and lecturer in 2014 at Osaka Prefecture University. His research interests include metal complex catalysts, bioactive complexes, and heteroatom-containing conjugated chemistry.

ship with Richard H. Holm at Harvard University in 1995. His research interests include metal complexes, crystal structure chemistry, and bioactive complexes.

Women's University, where he is full professor. In 2004, he moved as full professor to the Department of Applied Chemistry at Osaka Prefecture University. His research interests are organic synthesis, heteroatom chemistry, organometallic chemistry, and green chemistry. Downloaded by: Flinders University of South Australia. Copyrighted material





K. Marui et al.

In our initial study directed at green oxidation, 3-hydroxypicolinic acid (H_2 hpic) was used as a ligand for oxovanadium in the catalytic oxidation of benzylic alcohols (Equation 2).¹¹ 3-Hydroxypicolinic acid contains polar entities, such as hydroxy, hydroxycarbonyl, and pyridyl groups, and, therefore, was expected to have a good affinity toward water. The vanadium–3-hydroxypicolinic acid complex [VO(Hhpic)₂] can be easily synthesized from vanadium(IV) oxide sulfate (VOSO₄) and 3-hydroxypicolinic acid.¹²





As seen in Equation 2, the oxidation reaction required the use of pressurized oxygen and the organic solvent acetonitrile, with heating at high temperatures. To accomplish the catalytic oxidation under an atmosphere of oxygen (or air), and in water, detailed investigations regarding the optimization of the vanadium catalyst were conducted, and, finally, the aerobic oxidation of benzyl alcohols in water was developed, using 4,4'-di-*tert*-butylbipyridyl (*t*-Bubpy) as the ligand for oxovanadium, as shown in Equation 1.⁶

Since we could develop a good example of green oxidation of benzylic alcohols by using the vanadium catalyst $[VO(t-Bubpy)_2]$, we next investigated the eco-friendly oxidation of amines to imines (Table 1). At first, oxidation of benzylamine (1a) was examined using the vanadium-3-hydroxypicolinic acid complex [VO(Hhpic)₂].¹³ Under molecular oxygen (1.0 MPa), in acetonitrile, and at 120 °C for 6 h in a stainless steel autoclave, *N*-benzylbenzylideneamine (2a) was obtained successfully in 80% yield (entry 1). The formation of 2a can be reasonably explained by the oxidative dehydrogenation of benzylamine (1a) to generate benzylideneamine (PhCH=NH), followed by amino group exchange between benzylideneamine and benzylamine (1a) (Scheme 1). Decreasing the oxygen pressure resulted in a decrease in the yield of imine 2a (entries 3-5); interestingly, however, even under 0.1 MPa of oxygen, the oxidation proceeded to afford 2a in 48% yield (entry 5). The oxidation did not take place under air (entry 6). Decreasing the temperature resulted in decreased yields of 2a, indicating that the oxidation required heating over 100 °C (entries 7 and 8). Bubbling with oxygen was not effective for the oxidation (entry 9). Prolonging the reaction time successfully facilitated atmospheric oxidation of benzylamine (1a) to afford 2a in 86% yield (entry 10). Next, other vanadium catalysts were examined for the oxidation of amines under pressurized or atmospheric oxygen (entries 11-18). Among the catalysts examined, the vanadium complex [VO(Hhpic)₂] exhibited the best results (entry 10). In the absence of a catalyst, no reaction was observed (entry 19).

NH ₂	cat. (2.0 mol%), O ₂		\searrow
	MeCN (6.0 mL)		
1a (1 5 mmol)		20	

Entry	Catalyst	02	Temp (°C)	Time (h)	Yield ^ь (%)
1	[VO(Hhpic) ₂]	1.0 MPa	120	6	80
2		1.0 MPa	100	3	79
3		0.5 MPa	120	6	67
4		0.3 MPa	120	6	60
5		0.1 MPa	120	6	48
6		air (0.1 MPa)	120	6	NR
7		0.1 MPa	100	6	26
8		0.1 MPa	70	6	NR
9		O ₂ bubbling	70	6	NR
10		0.1 MPa	120	18	86
11	[VO(acac) ₂]	1.0 MPa	100	3	trace
12		0.1 MPa	120	18	34
13	V ₂ O ₅ (1 mol%)	1.0 MPa	100	3	13
14		0.1 MPa	120	18	30
15	VOSO ₄	1.0 MPa	100	3	7
16		0.1 MPa	120	18	30
17	$[VO{OCO(CH_2)_{16}Me}_2]$	1.0 MPa	100	3	50
18	[VO(OEt) ₃]	1.0 MPa	100	3	25
19	none	0.1 MPa	120	18	NR

 $^{\rm a}$ Reactions were carried out in a stainless autoclave with magnetic stirring under O_2 (0.1 MPa).

^b Yields were determined by ¹H NMR; NR = no reaction.



With the optimized conditions (Table 1, entry 10) in hand, the catalytic oxidation of various benzylamine derivatives **1** was examined using the vanadium complex $[VO(Hhpic)_2]$ as the catalyst, and these results are shown in Table 2. Oxidation of *p*-substituted benzylamines **1b**–**d** afforded the corresponding imines **2b**–**d** in good yields (entries 1–3). Although benzylic primary amines **1** underwent dehydrogenative condensation to give *N*-benzylbenzylideneamine derivatives **2**, secondary amines such as dibenzyl-

Syn<mark>thesis</mark>

amine (**1e**) underwent oxidative dehydrogenation to afford the corresponding imines. For example, catalytic oxidation of dibenzylamine (**1e**) gave *N*-benzylbenzylideneamine (**2a**) in moderate yield (entry 4). In the case of 1,2,3,4-tetrahydroisoquinoline (**1f**), 3,4-dihydroisoquinoline (**2f**) was successfully obtained in good yield (entry 5). Interestingly, the oxidation of tertiary amine **1g** afforded *N*-benzylideneaniline (**2g**) in good yield via the elimination of a benzyl group (entry 6). In this reaction, the eliminated benzyl group was converted into benzaldehyde (75%, ¹H NMR vield) via oxidation.

K. Marui et al.



 $^{\rm a}$ Reactions were carried out in a stainless autoclave with magnetic stirring under O_2 (0.1 MPa).

^b Isolated yield.

^c Yields were determined by ¹H NMR.

^d Amine **1e** was recovered (58%).

The oxidation in acetonitrile catalyzed by the vanadium complex $[VO(Hhpic)_2]$ required the use of a stainless steel autoclave, because of heating at 120 °C, even though the oxygen pressure was only 0.1 MPa.

Ionic liquids are useful eco-friendly solvents and suitable for recycling of both the ionic liquid itself and the catalyst.¹⁴ Furthermore, various organic and inorganic compounds have good solubility in ionic liquids, which do not vaporize over 120 °C. Therefore, the oxidation could be conducted in a normal glass vessel when an ionic liquid is used as the solvent. Thus, we examined the oxidation of benzylamines **1** in ionic liquids under oxygen, catalyzed by the vanadium complex $[VO(Hhpic)_2]$ (Table 3).

Table 3 Oxidation of Benzylamines 1 in Various Ionic Liquids^a

٨	VO(Hhp	nic) ₂ (2 mol%), O ₂ (0.1 MI	^D a) Ar	≪ _N ∕∕_ _{Ar}
Ar	ionic liqu	uid (2.0 mL), 120 °C, 6.0	h	
1 (1.	5 mmol)			2
Entry	Ionic Liquid	Substrate 1	Product 2	Yield ^b (%)
1	Me N PF	Hex G 6 1a	2a	75
2 ^c		1b	2b	73
3°		1d	2d	51
4 ^{c,d}		1e	2a	33
5		Bu 1a 6	2a	46
6		Bu ⊖ 1a ₄	2a	43
7		Et ⊝ 1a ₄	2a	18
8		Et ⊝ 1a	2a	12
9		Et Domentia	2a	10

^a Reactions were carried out in a glass vessel under O_2 (0.1 MPa).

^b Yields were determined by ¹H NMR.

^c Substrate (1.0 mmol)

^d After a reaction time of 20 h, **1e** was recovered (53%).

The yields of **2a** were influenced by both the cation and the anion of the tested ionic liquids. Among the ionic liquids employed, 1-hexyl-3-methylimidazolium hexafluorophosphate {[hmim]PF₆} was found to be the most suitable for the oxidation of **1a**, and it was possible to conduct the oxidation in a glass vessel (entry 1). Oxidation of *p*-substituted benzylamines **1b** and **1d** was also successful, and the corresponding imines **2b** and **2d** were obtained in 73% and 51% yields, respectively (entries 2 and 3). In the case of dibenzylamine (**1e**), oxidative dehydrogenation took place to give imine **2a** in 33% yield.

Next, we investigated the recyclability of the catalyst in the ionic liquid [hmim]PF₆ (see Figure 1); the results are shown in Table 4. Both the substrate and catalyst easily dissolved in the ionic liquid, and the oxidation (Ox.) could be performed as a homogeneous reaction. After the reaction

(entry 1, 1st run), the product was easily extracted with diethyl ether, and the ionic liquid layer, which contained the vanadium complex $[VO(Hhpic)_2]$, was used for the next run (Figure 1). The result showed that the ionic liquid solvent [hmim]PF₆ containing the vanadium complex $[VO(Hhpic)_2]$ was successfully reused (entry 1, 2nd run). In the third run (entry 1, run 3), we attempted the oxidation under air, and the desired imine **2a** was obtained in moderate yield. In the fourth run (entry 1, run 4), the oxidation was performed again under an oxygen atmosphere, and **2a** was obtained in good yield without any detectable loss in catalytic activity.



Figure 1 Reuse of ionic liquid (IL) and catalyst

 Table 4
 Recycling Study of Vanadium Complex [VO(Hhpic)₂] in Ionic Liquid

1a (1.5 mmo	`NH₂ ⊳I)	۷ ۲ [۱ ۱	/O(Hhpid D ₂ (0.1 M nmim]PF 20 °C, 6	c) ₂ (2 n IPa) 5 ₆ (2.0 n	nol%) 	- [Y	∕∼ <mark>∧</mark> ∕∕ 2a	
Entry	Run	Recyc	ling rur	I					
Entry 1	1	2	3	4					
Yield (%) ^{a,b}	75	66	48 ^c	69					
Entry 2	1	2	3	4	5	6	7	8	9
Yield (%) ^{a,b}	69	70	64	67	68	66	56	58	68 (67)

^a Yields were determined by ¹H NMR (isolated yield given in parentheses).

^b Starting benzylamine still remained, but no byproduct was detected.

^c The oxidation was carried out under air.

The oxidation of **1a** under oxygen was examined (Table 4, entry 2), and the catalyst could be successfully recycled more than nine times. Conceivably, coating the catalyst with ionic liquid may prevent aggregation of the catalyst, making it possible to maintain the catalytic activity over several reaction cycles. Overall, the vanadium complex $[VO(Hhpic)_2]$ is a highly effective and recyclable catalyst for the oxidation of benzylamines to the corresponding imines with molecular oxygen in ionic liquids such as $[hmim]PF_6$.

In addition to molecular oxygen, hydrogen peroxide is an alternative eco-friendly oxidant that is used in organic synthesis and industrial chemistry, because it is inexpensive, safe at low concentrations (<30% aqueous H_2O_2), and affords water as the only byproduct after oxidation. When hydrogen peroxide is employed as an oxidant, water is one of the most suitable solvents. The use of water instead of organic solvents is advantageous, as it is inexpensive, non-toxic, and nonflammable. Furthermore, to achieve a low-carbon society, it is necessary to reduce the use of organic solvents. Thus, we investigated the catalytic oxidation of amines with hydrogen peroxide in water.¹⁵

At first, the vanadium(IV) oxide sulfate catalyzed oxidation of amine **1a** with hydrogen peroxide in water at room temperature was investigated. However, product **2a** was obtained in only 2% yield (Table 5, entry 1). Oxovanadium bearing 3-hydroxypicolinic acid or 4,4'-di-*tert*-butylbipyridyl were also ineffective in this oxidation (entries 2 and 3). Thus, we examined the catalytic oxidation of benzylamine (**1a**) in the presence of various metal sulfates [MSO₄, M = Fe, Co, Ni, Cu, Zn and Ce(SO₄)₂] as catalysts. Although most metal sulfates exhibited minimal catalytic activities in the oxidation (the yields of **2a** were 1–3%), copper(II) sulfate catalyzed the reaction efficiently, and **2a** was obtained in a high yield (entry 4).^{16,17}

\bigcirc	Catalyst (0.2 mo NH ₂ H ₂ O ₂ (2.0 mmol H ₂ O (2.0 mL), r.	%)) t., 2.0 h	N I
1a (2.0 r	nmol)		2a
Entry	Catalyst	Yield ^b (%)	
		2a	1a (recovery)
1	VOSO ₄ ·5H ₂ O	2	63
2	VO(Hhpic) ₂	2	96
3	VO(t-Bubpy) ₂	2	95
4	CuSO ₄ ·5H ₂ O	88	4
5°	none	1	89
6	CuCl	38	36
7	CuBr	30	46
8	Cul	49	24
9	Cu(CH ₃ COO) ₂ ·H ₂ O	52	20
10	$Cu(NO_3)_2 \cdot 6H_2O$	54	23
11	Cu(CF ₃ SO ₃) ₂ ·H ₂ O	63	14
12 ^d	CuSO ₄ ·5H ₂ O	trace	93

^a Aqueous solution of H_2O_2 (10%) was used.

^b Yields were determined by ¹H NMR; yield of imine **2a** is based on substrate **1a**.

^c Reaction time 3 h.

^d Amine **1a** (1.0 mmol), CuSO₄ (0.01 mmol, 1.0 mol%), H₂O (1.0 mL), 24 h,

 O_2 balloon, in the absence of H_2O_2 .

A negligible yield of imine **2a** was obtained when no catalyst was used (Table 5, entry 5). Various copper(I) and copper(II) salts were examined in the oxidation, giving imine **2a** in poor to high yields, with recovery of the starting amine (entries 6-11). On the other hand, the desired

 Table 5
 Oxidation of Benzylamine (1a) in the Presence of Various Metal Catalysts^a

amine oxidation did not take place under oxygen in the absence of hydrogen peroxide (entry 12). Overall, copper(II) sulfate was the best catalyst for the oxidation of amine **1a** to imine **2a** with hydrogen peroxide.

The oxidation of substituted benzylamines 1 with hydrogen peroxide in water at room temperature was investigated using copper(II) sulfate as the catalyst (Table 6). The oxidation of benzylamine (1a) proceeded very smoothly, and was complete within 1.5 hours (entries 1 and 2). Chloro, methyl, methoxy, trifluoromethyl, and tert-butyl groups were all tolerated in the catalytic oxidation, affording the corresponding imine derivatives 2 in good to high yields (entries 3-13). In the cases of amines 1b, 1d, 1h, and **1i**, the use of 0.5–1.0 mol% of the catalyst resulted in higher vields of the imines, and the isolated vields are shown in parentheses. In contrast, the oxidation of secondary amines such as dibenzylamine (1e) and 1,2,3,4-tetrahydroisoquinoline (1f) did not proceed, probably because oxidative dehydrogenation of secondary amines requires the use of higher reaction temperatures (entries 14 and 15).

In general, aliphatic amines are oxidized less efficiently than the corresponding aromatic amines. Very interestingly, this mild oxidation method could, nevertheless, be applied successfully to aliphatic amines; aliphatic primary amines **11**, **1m**, and **1n** were also efficiently oxidized to the corresponding imines **2l**, **2m**, and **2n** (Table 6, entries 16–18).

Since the copper(II) sulfate catalyzed oxidation proceeded under very mild reaction conditions, we next investigated the cross condensation of two amines. When the oxidation of equimolar amounts of benzylamine (1a) and hexylamine (11) with hydrogen peroxide was examined in the presence of copper(II) sulfate (0.2 mol%) in water at room temperature for 1.5 hours, two types of cross-condensed imine derivatives 3a and 3a' were obtained in 26% and 6% yields, respectively, along with the homo-condensed product 2a (30%) (Equation 3). Despite our efforts, the selective formation of **3a** could not be attained. To inhibit the formation of the regioisomer (e.g., 3a'), the oxidative cross condensation was performed using aromatic amines such as aniline (PhNH₂, **10**) instead of hexylamine **11**. Owing to the decreased nucleophilicity of aniline, however, the formation of cross-condensed products such as N-phenylbenzylideneamine (PhCH=NPh, 2g) was not observed, even when an excess of aniline was used.

Thus, we next examined cross condensation accompanied by cyclization. After the copper(II) sulfate catalyzed oxidation of benzylamine (**1a**) with hydrogen peroxide in water was conducted at room temperature for 1.5 hours, *o*phenylenediamine (**1p**) was added to the resulting mixture, and the reaction was continued with heating at 100 °C for 20 hours. The reaction successfully afforded 2-phenylbenzimidazole (**3b**) in a moderate yield (Equation 4).



36

	Ar NH ₂ —	CuSO ₄ H ₂ O ₂ (2.0) mmol)		Ar N	Ar
	1 (2.0 mmol)	H ₂ O (2.0	mL), r.t.	, 1.5 h	2	
					-	
ntry	Substrate 1			CuSO ₄ (mol%)	Product 2	Yield [®] (%)
1 ^c	NH ₂		1a	0.2	7a	84
2			i a	0.2	24	91 (72)
3		NH ₂	11.	0.2	21	78
4	CI CI		ID	0.5	20	85 (84)
5	Me	NH ₂	1c	0.2	2c	74 (71)
6 ^c	\sim	NH₂		0.2		71
7	MeO		1d	0.5	2d	87 (76)
8	MeO			0.2		62
9		NF12	1h	0.5	2h	99 (90)
10				0.2		67
11	OMe		1i	1.0	2i	81 (66)
12	F ₃ C	NH ₂	1j	0.2	2j	78 (70)
13 ^d	^t Bu	NH ₂	1k	0.2	2k	82 (66)
14	Ph N Ph	I	1e	0.2	2a	trace
15	NH		1f	0.2	2f	ND
16	\sim	NH ₂	11	0.2	21	75
17	\sim	NH ₂	1m	0.2	2m	85
18 ^d	NH ₂		1n	0.2	2n	74 (57)

^a Aqueous solution of H_2O_2 (10%) was used.

^b Yields were determined by ¹H NMR yield (isolated yield in parentheses); yield of **2** is based on substrate **1**. ND = not determined.

Reaction time 1.0 h

^d H₂O₂ (3.0 mmol) was used.

This result prompted us to examine the one-pot oxidative condensation of benzylamine (**1a**) with *o*-substituted aniline derivatives. Thus, we selected *o*-sulfanylaniline (**1q**) as a condensation partner, and one-pot oxidation and cyclization reactions were examined using 1.0 mol% of copper(II) sulfate in water with heating at 100 °C (Equation 5). Heating of 1.5 equivalents of benzylamine (**1a**) with *o*-sulfanylaniline (**1q**) for 20 hours resulted in the desired oxida-

K. Marui et al.

37



Equation 3 Oxidative cross condensation of benzylamine (1a) with hexylamine (1I)







Equation 5 Oxidative condensation and cyclization of benzylamine (1a) with o-sulfanylaniline (1q)

tion and cyclization to directly afford 2-phenylbenzothiazole (3c) in 71% yield. Notably, the same reaction occurred when oxygen was used as the oxidant instead of hydrogen peroxide.¹⁸

Thus, the copper(II) sulfate catalyzed oxidation can be easily performed, and the oxidation of amines to the corresponding imines can be carried out at room temperature in 1.5 hours under mild conditions by using hydrogen peroxide in water. In addition, the method can be applied to the synthesis of *N*-containing heterocycles.

Since a method with a good catalyst and very mild catalytic oxidation conditions could be developed, we next investigated energetically useful oxidation systems. For environmentally benign oxidation reactions using photoenergy such as sunlight as the driving force, metal complexes with strong absorption in the visible region and high electrontransfer abilities are required. Chlorins are suitable photocatalysts owing to their strong photoabsorption properties; moreover, they can form complexes with various metals, affording metallochlorins with desirable electron-transfer abilities. To the best of our knowledge, the oxidation of amines catalyzed by metallochlorins has rarely been reported.^{19,20} Thus, we investigated the oxidation of benzylamine (1a) in the presence of oxovanadium(IV)-chlorin derivative 4 and zinc(II)-chlorin 5 [Zn(TFPC)] as photocatalysts in ethanol or benzotrifluoride (BTF). Benzotrifluoride has attracted significant attention as an eco-friendly solvent in organic synthesis, as it can be used as a replacement for typical organic solvents such as toluene, benzene, and dichloromethane because of its low toxicity and suitable polarity. The reaction mixture was photoirradiated using a xenon lamp through a Pyrex glass vessel (hv > 300 nm), and oxygen gas was introduced into the flask upon connection to an oxygen balloon. After one hour, the reaction mixture was extracted with diethyl ether, and the products were characterized by ¹H NMR spectroscopy (Equation 6).



Equation 6 Oxidation reaction in the presence of photocatalyst **4** or **5**. ^a In the dark.

In ethanol or benzotrifluoride, photocatalysts **4** and **5** successfully catalyzed the oxidation of amine **1a** to imine **2a** in good yields. Compared to the catalytic activity of vanadium complex **4**, zinc complex **5** exhibited higher catalytic activity, and the corresponding imine (**2a**) was obtained in 97% yield. Therefore, zinc complex **5** was used as the oxidation catalyst in subsequent experiments. The reaction did not proceed in the dark, indicating that photoirradiation was indispensable for this oxidation reaction.

Next, the photoinduced amine oxidation was carried out under various conditions (Table 7). When acetonitrile, toluene, and tetrahydrofuran were used as the solvent, product **2a** was obtained in excellent yields (entries 2–4), similar to that when the reaction was carried out in benzotrifluoride (entry 1). When the reaction time was shortened, the product yield decreased somewhat (entry 5). The reaction did not proceed in the absence of the photocatalyst or oxygen (entries 6 and 7). The photoirradiation of amine **1a** using a tungsten lamp through Pyrex (hv > 300 nm) afforded imine **2a** in 90% yield (entry 8). When a xenon lamp was used through a glass filter (hv > 400 nm), imine **2a** was obtained in an excellent yield (entry 9).

Syn<mark>thesis</mark>

K. Marui et al.



1a (0.5 mi	NH ₂ 5 (0.2 mol?) NH ₂ O ₂ (0.1 MF Xe lamp (<i>h</i> solvent (1.0	(%) Pa) N >300 nm) 0 mL), r.t. 2	a
Entry	Solvent	Time (h)	Yieldª (%)
1	BTF	1	97
2	MeCN	1	93
3	toluene	1	95
4	THF	1	81
5	BTF	0.5	81
6 ^b	BTF	1	1
7 ^c	BTF	1	3
8 ^d	BTF	3	90
9 ^e	BTF	1	97

^a Yield determined by ¹H NMR.

^b No catalyst was used.

 $^{\circ}$ N₂ (0.1 MPa) was used.

^d Tungsten lamp was used.

^e Xe lamp through a glass filter (*h*v >400 nm) was used.

The photoinduced oxidation of various benzylamines 1 was also carried out using a xenon lamp through Pyrex (Table 8). The oxidation of benzylamines 1 with diverse substituents such as *p*-chloro, *p*-methyl, *p*-methoxy, *m*-methoxy, and *p-tert*-butyl afforded the corresponding *N*-benzylbenzylideneamines 2 in excellent yields (entries 1, 2, 3, 6, and 9). The oxidation of benzylamines containing o-methoxy and *p*-trifluoromethyl groups as electron-donating and -withdrawing substituents, respectively (entries 4 and 7), was completed in 1.5 hours, affording the corresponding imines 2i and 2j in excellent yields (entries 5 and 8). The oxidation of dibenzylamine (1e), a secondary amine, afforded the corresponding imine 2a in 90% yield (entry 10). The results clearly indicate that the oxidizing ability of the photocatalyst toward secondary amines is greater than that of copper(II) sulfate.

The photoinduced oxidation of amine **1f** afforded a mixture of three oxidation products, namely **2f**, **6**, and **7** (Table 9, entries 1–3). Monitoring the reaction by ¹H NMR spectroscopy revealed that the desired product **2f** was gradually converted into **7**, probably by reaction with water. Therefore, 4 Å molecular sieves (MS4A) were added to the reaction mixture; this afforded imine **2f** in very good yield without formation of **7** (entry 4). This reaction also took place when a tungsten lamp was used as the light source (entry 5).

Next, the oxidation of hexylamine (**1I**), an aliphatic amine, was investigated (Equation 7). However, a complex mixture was obtained. When 4 Å molecular sieves were used, the reaction afforded the desired imine **2I** in good yield.

Feature



38

		5 (0.2 mol% O ₂ (0.1 MPa) a)			
	Ar NH ₂ —	Xe lamp (<i>h</i> BTF (1.0 ml	/ >300 r L), r.t.	ım)	Ar' N 2	`Ar
Entry	Substrate 1			Time (h)	Product 2	Yieldª (%)
1	CI	NH ₂	1b	1.0	2b	92
2	Me	NH ₂	1c	1.0	2c	95
3	MeO	NH ₂	1d	1.0	2d	96
4	NH ₂			1.0	- .	58
5	OMe		п	1.5	21	99
6	MeO	NH ₂	1h	1.0	2h	95
7	\sim	`NH₂		1.0		77
8	F ₃ C		1j	1.5	2j	98
9	^t Bu	`NH ₂	1k	1.0	2k	97
10	Ph N Ph		1e	1.0	2a	90

^a Yields were determined by ¹H NMR.



Equation 7 Oxidation of amine 11. ^a Determined by ¹H NMR.

Finally, this method was applied to the oxidation of benzylamines **1** in open air (Table 10). The oxidation of benzylamines **1a**, **1i**, and **1j** afforded the corresponding imines **2a**, **2i**, and **2j** in excellent yields.

Although further detailed mechanistic experiments are required to elucidate the true mechanism, a possible pathway for the presented photoinduced oxidation of amines is shown in Scheme 2. The reaction of the photoactivated zinc-chlorin catalyst **5** [Zn(TFPC)] with molecular oxygen generates singlet oxygen (**8**); subsequent electron transfer from the amine results in the formation of a radical cation **9** and superoxide (**10**). Abstraction of a proton from the radi-

K. Marui et al.

39

Table 9 Photo	oinduced Ox	idation of Amiı	ne 1f	
	5 (0.2 mo O ₂ (0.1 N	I%) IPa)		
1f (0.5 mmol)	Xe lamp (BTF (1.0	(<i>h</i> v >300 nm) mL), r.t.	-	
		• • • •	NH +	NH O
		2f	6	7
Entry	Time (h)	Yieldª (%)		
		2f	6	7
1	0.5	47	3	13
2	1.0	11	12	40
3 ^b	1.5	0	13	36
4 ^{c,d}	0.5	87	2	0
5 ^{c,e}	2.5	83	2	0

^a Yields were determined by ¹H NMR.

^b Complex mixture.

^c MS4A (100 mg) was used.

^d Xe lamp through a glass filter (hv >400 nm) was used.

^e Tungsten lamp was used.

Table	10 Oxidation of	Amines 1 under Air ^a		
		4 (0.2 mol%) air (0.1 MPa)		
	1 (0.5 mmol)	Xe lamp (<i>h</i> v >400 nm) BTF (1.0 mL), r.t.	2	
Entry	Substrate	1 Time (h)	Product 2	Yield ^b (%)
1	1a	1.5	2a	97
2	1i	2.0	2i	91
3	1j	2.0	2j	90

^a Through a glass filter (*h*v >400 nm). ^b Yields were determined by ¹H NMR.

cal cation **9** by superoxide, followed by hydrogen absorption, leads to N-unsubstituted imine **11** and hydrogen peroxide. Nucleophilic substitution of imine **11** with another molecule of the amine affords an N-substituted amine. Then, **2a** is formed with concomitant formation of ammonia.



Scheme 2 Possible reaction pathway of the photoinduced oxidation of amines

In summary, a series of eco-friendly oxidation reactions of amines to form the corresponding imines was developed. Firstly, we found that the vanadium complex [VO(Hhpic)₂] is a highly effective catalyst for the selective oxidation of benzylamines to the corresponding imines by molecular oxygen in acetonitrile. In addition, in ionic liquids the vanadium complex [VO(Hhpic)₂] could be employed as a reusable catalyst for the oxidation of benzylamines to imines. Secondly, copper(II) sulfate catalyzed oxidation of amines to the corresponding imines was developed. The method is simple to perform, and the oxidation of the amines to the corresponding imines proceeds under very mild conditions, with hydrogen peroxide used in water at room temperature. Finally, we found that the photoinduced oxidation of amines to imines using a zinc(II)-chlorin complex as the photocatalyst proceeds under mild conditions, with oxygen or air used as oxidant, in benzotrifluoride at room temperature. Photoenergy was successfully employed as the driving force, and primary and secondary amines were oxidized to the corresponding imines in excellent yields. These novel oxidation methods are expected to facilitate the development of the green oxidation of other functional groups.

¹H NMR (300 or 400 MHz) and ¹³C NMR (75 or 100 MHz) spectra were recorded on JEOL JNM–ALICE, JEOL JNM–ECX FT NMR, or JEOL JNM–ECS FT NMR spectrometers of samples in CDCl₃ at room temperature. The chemical shifts are reported in parts per million downfield from tetramethylsilane (δ = 0.0 ppm) as internal standard for ¹H NMR or CDCl₃ (δ = 77.0 ppm) for ¹³C NMR. Melting points were determined using a Yanaco MP-J3 instrument. [VO(Hhpic)₂] was prepared following a published procedure.¹² 1-Hexyl-3-methylimidazolium hexafluorophosphate {[hmim]PF₆} was synthesized and characterized according to a published procedure.²¹ MeCN was distilled over CaH₂ prior to

Feature

K. Marui et al.

use. Unless otherwise noted, other reactants and reagents were purchased from commercial sources and were used as received without further purification.

Imines 2 by Vanadium-Catalyzed Oxidation of Benzylamines 1 in Sealed Equipment (Tables 1 and 2); General Procedure 1

The reactions were carried out in a stainless steel autoclave (50 mL). The vanadium catalyst (0.03 mmol), amine **1** (1.5 mmol), and MeCN (6 mL) were added sequentially to the autoclave, and O_2 was introduced (0.1 MPa). The autoclave was placed over an oil bath (120 °C), and the reaction mixture was stirred magnetically for the desired reaction time. The reaction mixture was filtered through Celite and washed with Et₂O. After evaporation of the solvent, the crude product was purified by column chromatography (silica gel, hexane–EtOAc); this afforded the corresponding analytically pure imines **2**.

Imines 2 by [VO(Hhpic)₂]-Catalyzed Oxidation of Benzylamines 1 in Ionic Liquids (Table 3); General Procedure 2

A mixture of $[VO(Hhpic)_2]$ (10.3 mg, 0.03 mmol), benzylamine **1** (160.7 mg, 1.5 mmol), and ionic liquid (2 mL) was added to a 30 mL two-necked glass vessel, stirred, and heated at 120 °C for 6 h under atmospheric O₂. The reaction mixture was extracted with Et₂O. The extract was concentrated under vacuum. The product was characterized by ¹H NMR; 1,2-diphenylethane was used as the internal standard.

Recycling of the Catalyst in [hmim]PF₆ (Table 4)

The first cycle was performed following general procedure 2, using [hmim]PF₆ as the solvent. After the products were separated from [hmim]PF₆ by extraction with Et₂O, the [hmim]PF₆ layer containing the catalyst was dried in vacuo for 6 h. The resulting ionic liquid layer was used for the next oxidation reaction upon adding benzylamine (**1a**; 1.5 mmol).

Imines 2 by CuSO₄-Catalyzed Oxidation of Amines 1 (Equations 3– 4, Tables 5 and 6); General Procedure 3

Amine **1** (2.0 mmol), $CuSO_4 \cdot 5H_2O$ (1.0 mg, 0.004 mmol), and H_2O (2.0 mL) were added to a two-necked glass vessel. A 10% aqueous solution of H_2O_2 was added dropwise to the mixture under stirring. After the appropriate reaction time, the product was extracted with Et_2O . The organic layer was dried (MgSO₄), filtered, and concentrated. The product was dissolved in $CDCl_3$, and an appropriate amount of 1,3,5-trioxane was added as the internal standard to determine the yield of the product by ¹H NMR. The products were purified by passing through a short pad of silica gel (Wakogel C-200; EtOAc-hexane-Et₃N) or by gel permeation chromatography (GPC); this affording the corresponding analytically pure imine **2**. Silica gel was carefully dried in vacuo prior to use, because the H₂O in silica gel reacted with the imine product. Products **2m** and **2n** could not be purified satisfactorily by chromatography owing to hydrolysis.

Oxidation of Amines 1 Catalyzed by a Photocatalyst (Equations 6 and 7, Tables 7–10); General Procedure 4

Fluorinated chlorins were prepared and metalated according to reported methods, to provide catalysts **4** and **5**.²² Amine **1** (0.5 mmol) and photocatalyst **4** or **5** (0.001 mmol) were added to BTF (1.0 mL) in a two-necked Pyrex glass vessel. O₂ gas was introduced into the vessel by connecting an O₂ balloon, and the reaction mixture was stirred and irradiated using a Xe lamp through Pyrex (hv > 300 nm) for 1 h. After extraction of the reaction mixture with Et₂O, the organic layer

N-Benzylbenzylideneamine (2a) (Table 6, entry 2)

Purification by column chromatography (silica gel, hexane-EtOAc- Et_3N , 80:19:1).

Yield: 140.6 mg (72%); colorless oil.

 ^1H NMR (400 MHz, CDCl_3): δ = 8.36 (s, 1 H), 7.78–7.76 (m, 2 H), 7.40–7.22 (m, 8 H), 4.80 (s, 2 H).

¹³C NMR (100 MHz, CDCl₃): δ = 161.88, 139.22, 136.08, 130.67, 128.51, 128.41, 128.20, 127.89, 126.89, 64.95.

HRMS: *m*/*z* [M]⁺ calcd for C₁₄H₁₃N:195.1048; found: 195.1044.

N-(4-Chlorobenzyl)-4-chlorobenzylideneamine (2b) (Table 6, entry 4).

Purification by column chromatography (silica gel, hexane-EtOAc- Et_3N , 80:19:1).

Yield: 222.7 mg (84%); white solid; mp 64-65 °C.

¹H NMR (400 MHz, CDCl₃): δ = 8.31 (s, 1 H), 7.70–7.68 (m, 2 H), 7.39–7.36 (m, 2 H), 7.31–7.24 (m, *J* = 8.6 Hz, 4 H), 4.75 (s, 2 H).

 ^{13}C NMR (100 MHz, CDCl₃): δ = 160.76, 137.57, 136.81, 134.41, 132.76, 129.40, 129.20, 128.87, 128.57, 64.10.

HRMS: *m*/*z* [M]⁺ calcd for C₁₄H₁₁Cl₂N: 263.0269; found: 263.0262.

N-(4-Methylbenzyl)-4-methylbenzylideneamine (2c) (Table 6, entry 5)

Purification by column chromatography (silica gel, hexane-EtOAc- Et_3N , 80:19:1).

Yield: 157.8 mg (71%); pale yellow solid; mp 83-84 °C.

¹H NMR (400 MHz, CDCl₃): δ = 8.32 (s, 1 H), 7.65 (d, *J* = 8.2 Hz, 2 H), 7.22–7.19 (m, 4 H), 7.13 (d, *J* = 8.2 Hz, 2 H), 4.75 (s, 2 H), 2.36 (s, 3 H), 2.32 (s, 3 H).

 ^{13}C NMR (100 MHz, CDCl_3): δ = 161.62, 140.90, 136.44, 136.31, 133.57, 129.24, 129.10, 128.19, 127.90, 64.75, 21.45, 21.05.

HRMS: *m*/*z* [M]⁺ calcd for C₁₆H₁₇N:223.1361; found: 223.1359.

N-(4-Methoxybenzyl)-4-methoxybenzylideneamine (2d) (Table 6, entry 7)

Purification by GPC.

Yield: 192.9 mg (76%); pale yellow oil.

¹H NMR (400 MHz, CDCl₃): δ = 8.27 (s, 1 H), 7.70 (d, J = 8.7 Hz, 2 H), 7.23 (d, J = 8.7 Hz, 2 H), 6.90 (d, J = 8.7 Hz, 2 H), 6.87 (d, J = 8.7 Hz, 2 H), 4.71 (s, 2 H), 3.80 (s, 3 H), 3.77 (s, 3 H).

 ^{13}C NMR (100 MHz, CDCl₃): δ = 161.55, 160.82, 158.53, 131.56, 129.71, 129.06, 113.85, 113.78, 64.29, 55.22, 55.16.

HRMS: *m*/*z* [M]⁺ calcd for C₁₆H₁₇NO₂: 255.1259; found: 255.1261.

3,4-Dihydroisoquinoline (2f) (Table 2, entry 5)

Purification by column chromatography (silica gel, hexane-EtOAc- Et_3N , 75:24:1).

Yield: 155.7 mg (78%); pale yellow oil.

¹H NMR (CDCl₃, 300 MHz): δ = 8.32 (s, 1 H), 7.34 (m, 1 H), 7.28–7.26 (m, 2 H), 7.14 (d, J = 7.2 Hz, 1 H), 3.79–3.73 (m, 2 H), 2.73 (t, J = 7.3 Hz, 2 H).

¹³C NMR (CDCl₃, 75 MHz): δ = 160.29, 136.27, 131.02, 128.44, 127.38, 127.16, 127.03, 47.30, 24.97.

N-Benzylideneaniline (2g) (Table 2, entry 6)

Purification by column chromatography (silica gel, hexane-EtOAc- Et_3N , 80:19:1).

Yield: 203.9 mg (75%); pale yellow oil.

 ^1H NMR (CDCl_3, 300 MHz): δ = 8.40 (s, 1 H), 7.89–7.86 (m, 1 H), 7.44–7.34 (m, 5 H), 7.22–7.18 (m, 3 H).

 ^{13}C NMR (CDCl₃, 75 MHz): δ = 160.23, 151.97, 136.12, 131.26, 129.04, 128.70, 128.65, 125.83, 120.77, 54.05.

N-(3-Methoxybenzyl)-3-methoxybenzylideneamine (2h) (Table 6, entry 9)

Purification by column chromatography (silica gel, EtOAc–Et₃N, 99:1). Yield: 231.1 mg (90%); pale yellow oil.

¹H NMR (400 MHz, CDCl₃): δ = 8.26 (s, 1 H), 7.37 (s, 1 H), 7.26–7.19 (m, 3 H), 6.95–6.88 (m, 3 H), 6.78–6.75 (m, 1 H), 4.73 (s, 2 H), 3.74 (s, 3 H), 3.71 (s, 3 H).

 ^{13}C NMR (100 MHz, CDCl₃): δ = 161.68, 159.64, 159.53, 140.63, 137.34, 129.30, 129.22, 121.34, 120.03, 117.18, 113.40, 112.11, 111.51, 64.55, 54.97, 54.81.

N-(2-Methoxybenzyl)-2-methoxybenzylideneamine (2i) (Table 6, entry 11)

Purification by GPC.

Yield: 168.9 mg (66%); pale yellow oil.

¹H NMR (400 MHz, CDCl₃): δ = 8.84 (s, 1 H), 8.03 (dd, *J* = 7.8, 1.8 Hz, 1 H), 7.37–7.20 (m, 3 H), 6.98–6.84 (m, 4 H), 4.83 (s, 2 H), 3.83 (s, 3 H), 3.81 (s, 3 H).

 ^{13}C NMR (100 MHz, CDCl₃): δ = 158.66, 158.22, 156.95, 131.69, 129.01, 128.02, 127.82, 127.37, 124.75, 120.64, 120.40, 110.88, 110.07, 59.55, 55.40, 55.22.

HRMS: *m*/*z* [M]⁺ calcd for C₁₆H₁₇NO₂: 255.1259; found: 255.1260.

N-[4-(Trifluoromethyl)benzyl]-4-(trifluoromethyl)benzylideneamine (2j) (Table 6, entry 12)

Purification by GPC.

Yield: 231.2 mg (70%); pale yellow oil.

¹H NMR (400 MHz, CDCl₃): δ = 8.46 (s, 1 H), 7.90 (d, J = 8.2 Hz, 2 H), 7.68 (d, J = 8.2 Hz, 2 H), 7.61 (d, J = 8.2 Hz, 2 H), 7.47 (d, J = 7.7 Hz, 2 H), 4.89 (s, 2 H).

¹³C NMR (100 MHz, CDCl₃): δ = 161.1, 142.99, 138.97, 132.55 (q, J = 32.4 Hz), 129.40 (q, J = 32.4 Hz), 128.49, 128.10, 125.62 (q, J = 3.8 Hz), 125.46 (q, J = 3.8 Hz), 124.04 (q, J = 271.3 Hz), 64.37. HRMS: m/z [M]⁺ calcd for C₁₆H₁₁F₆N: 331.0796; found: 331.0793.

N-(4-*tert*-Butylbenzyl)-4-*tert*-butylbenzylideneamine (2k) (Table 6, entry 13)

Purification by GPC.

Yield: 202.6 mg (66%); yellow solid; mp 38-41 °C.

¹H NMR (400 MHz, CDCl₃): δ = 8.36 (s, 1 H), 7.71 (d, J = 8.2 Hz, 2 H), 7.43 (d, J = 8.2 Hz, 2 H), 7.35 (d, J = 8.2 Hz, 2 H), 7.26 (d, J = 8.7 Hz, 2 H), 4.76 (s, 2 H), 1.32 (s, 9 H), 1.31 (s, 9 H).

 ^{13}C NMR (100 MHz, CDCl_3): δ = 161.64, 154.05, 149.74, 136.41, 133.54, 128.04, 127.63, 125.48, 125.34, 64.78, 34.85, 34.42, 31.36, 31.19.

HRMS: *m*/*z* [M]⁺ calcd for C₂₂H₂₉N: 307.2300; found: 307.2293.

N-(Cyclohexylmethyl)cyclohexylmethyleneamine (2n) (Table 6, entry 18)

Purification by GPC.

Yield: 118.5 mg (57%); pale yellow oil.

 ^1H NMR (400 MHz, CDCl_3): δ = 7.42 (d, J = 4.6 Hz, 1 H), 3.18 (d, J = 6.4 Hz, 2 H), 2.20–2.12 (m, 1 H), 1.78–1.53 (m, 11 H), 1.35–1.08 (m, 8 H), 0.93–0.83 (m, 2 H).

 ^{13}C NMR (100 MHz, CDCl_3): δ = 168.69, 68.27, 43.31, 38.37, 31.15, 29.70, 26.47, 25.92, 25.87, 25.31.

HRMS: *m*/*z* [M]⁺ calcd for C₁₄H₂₅N: 207.1987; found: 207.1979.

Acknowledgment

This research was supported by a Grant-in-Aid for Exploratory Research (26620149), Scientific Research (C, No. 23550057), A-STEP, and Nanotechnology Platform Program of the Nara Institute of Science and Technology (NAIST) from the Ministry of Education, Culture, Sports, Science and Technology (MEXT), Japan. The authors also thank Professor S. Yano (NAIST) for synthetic support of catalysts and Professor M. Ueshima for his advice about oxidation reactions.

References

- (a) Thayer, A. M. Chem. Eng. News **1992**, 70 (10), 27. (b) Guo, Z.; Liu, B.; Zhang, Q.; Deng, W.; Wang, Y.; Yang, Y. Chem. Soc. Rev. **2014**, 43, 3480.
- (2) (a) Buchner, W.; Schliebs, R.; Winter, G.; Buchel, K. H. Industrielle Anorganische Chemie, 2nd ed.; VCH: Weinheim, 1986.
 (b) Delaude, L.; Laszlo, P. J. Org. Chem. 1996, 61, 6360.
- (3) (a) Noyori, R.; Aoki, M.; Sato, K. *Chem. Commun.* 2003, 1977.
 (b) Punniyamurthy, T.; Velusamy, S.; Iqbal, J. *Chem. Rev.* 2005, 105, 2329. (c) Shi, Z.; Zhang, C.; Tanga, C.; Jiao, N. *Chem. Soc. Rev.* 2012, 41, 3381. (d) Gunasekaran, N. *Adv. Synth. Catal.* 2015, 357, 1990.
- (4) (a) Shimizu, S.; Shimada, N.; Sasaki, Y. *Green Chem.* 2006, *8*, 608.
 (b) Shaughnessy, K. H. *Chem. Rev.* 2009, *10*9, 643. (c) Chanda, A.; Fokin, V. V. *Chem. Rev.* 2009, *10*9, 725. (d) Butler, R. N.; Coyne, A. G. *Chem. Rev.* 2010, *110*, 6302. (e) Simon, M.-O.; Li, C.-J. *Chem. Soc. Rev.* 2012, *41*, 1415.
- (5) (a) Mahyari, M.; Shaabani, A.; Behbahani, M.; Bagheri, A. Appl. Organomet. Chem. 2014, 28, 576. (b) Mahyari, M.; Shaabani, A. Appl. Catal., A 2014, 469, 524. (c) Nabid, M. R.; Bide, Y.; Aghaghafari, E.; Rezaei, S. J. T. Catal. Lett. 2014, 144, 355. (d) Jawale, D. V.; Gravel, E.; Villemin, E.; Shah, N.; Geertsen, V.; Namboothiri, I. N. N.; Doris, E. Chem. Commun. 2014, 50, 15251. (e) Ito, Y.; Ohta, H.; Yamada, Y. M. A.; Enoki, T.; Uozumi, Y. Tetrahedron 2014, 70, 6146. (f) Li, Y.; Gao, Y.; Yang, C. Chem. Commun. 2015, 51, 7721. (g) Huang, Z.; Li, F.; Chen, B.; Yuan, G. Green Chem. 2015, 17, 2325.
- (6) (a) Kodama, S.; Hashidate, S.; Nomoto, A.; Yano, S.; Ueshima, M.; Ogawa, A. *Chem. Lett.* **2011**, *40*, 495. (b) Marui, K.; Higashiura, Y.; Kodama, S.; Hashidate, S.; Nomoto, A.; Yano, S.; Ueshima, M.; Ogawa, A. *Tetrahedron* **2014**, *70*, 2431.

Syn<mark>thesis</mark>

K. Marui et al.

- (7) (a) Murahashi, S.-I. Angew. Chem. Int. Ed. 1995, 34, 2443.
 (b) Bloch, R. Chem. Rev. 1998, 98, 1407. (c) Adams, J. P. J. Chem. Soc., Perkin Trans. 1 2000, 125. (d) Kobayashi, S.; Mori, Y.; Fossey, J. S.; Salter, M. M. Chem. Rev. 2011, 111, 2626.
 (e) Largeron, M. Eur. J. Org. Chem. 2013, 5225. (f) Kataja, A. O.; Masson, G. Tetrahedron 2014, 70, 8783.
- (8) (a) Samec, J. S. M.; Éll, A. H.; Bäckvall, J.-E. Chem. Eur. J. 2005, 11, 2327. (b) Murahashi, S.-I.; Okano, Y.; Sato, H.; Nakae, T.; Komiya, N. Synlett 2007, 1675. (c) Landge, S. M.; Atanassova, V.; Thimmaiah, M.; Török, B. Tetrahedron Lett. 2007, 48, 5161. (d) Largeron, M.; Chiaroni, A.; Fleury, M.-B. Chem. Eur. J. 2008, 14, 996. (e) Zhu, B.; Lazar, M.; Trewyna, B. G.; Angelici, R. J. J. Catal. 2008, 260, 1. (f) Gnanaprakasam, B.; Zhang, J.; Milstein, D. Angew. Chem. Int. Ed. 2010, 49, 1468. (g) Kegnæs, S.; Mielby, J.; Mentzel, U. V.; Christensen, C. H.; Riisager, A. Green Chem. 2010, 12, 1437. (h) Huang, H.; Huang, J.; Liu, Y. M.; He, H. Y.; Cao, Y.; Fan, K. N. Green Chem. 2012, 14, 930. (i) Zhang, Z.; Wang, F.; Wang, M.; Xu, S.; Chen, H.; Zhang, C.; Xu, J. Green Chem. 2014, 16, 2523. (j) Chen, B.; Li, J.; Dai, W.; Wang, L.; Gao, S. Green Chem. 2014, 16, 3328. (k) Wendlandt, A. E.; Stahl, S. S. Org. Lett. 2012, 14, 2850. (1) Zhang, E.; Tian, H.; Xu, S.; Yu, X.; Xu, Q. Org. Lett. 2013, 15, 2704. (m) Han, L.; Xing, P.; Jiang, B. Org. Lett. 2014, 16, 3428. (n) Qin, Y.; Zhang, L.; Lv, J.; Luo, S.; Cheng, J.-P. Org. Lett. 2015, 17, 1469. (o) Wendlandt, A. E.: Stahl, S. S. I. Am. Chem. Soc. 2014, 136, 506. (p) Tayade, K. N.; Mishra, M. J. Mol. Catal. A: Chem. 2014, 382, 114. (q) Tanabe, Y.; Kuriyama, S.; Arashiba, K.; Nakajima, K.; Nishibayashi, Y. Organometallics 2014, 33, 5295. (r) Chen, B.; Wang, L.; Dai, W.; Shang, S.; Lv, Y.; Gao, S. ACS Catal. 2015, 5, 2788. (s) Biswas, S.; Dutta, B.; Mullick, K.; Kuo, C.-H.; Poyraz, A. S.; Suib, S. L. ACS Catal. 2015, 5, 4394. (t) Galletti, P.; Funiciello, F.; Soldati, R.; Giacominia, D. Adv. Synth. Catal. 2015, 357, 1840. (u) Rao, B. G.; Sudarsanam, P.; Rangaswamy, A.; Reddy, B. M. Catal. Lett. 2015, 145, 1436. (v) Largeron, M.; Fleury, M.-B. Chem. Eur. J. 2015, 21, 1.
- (9) (a) Yamazaki, S.; Yamazaki, Y. Bull. Chem. Soc. Jpn. 1990, 63, 301.
 (b) Kim, J. W.; Yamaguchi, K.; Mizuno, N. Angew. Chem. Int. Ed. 2008, 47, 9249.
- (10) Ogawa, A.; Curran, D. P. J. Org. Chem. 1997, 62, 450.
- (11) Kodama, S.; Ueta, Y.; Yoshida, J.; Nomoto, A.; Yano, S.; Ueshima, M.; Ogawa, A. *Dalton Trans.* **2009**, 9708.
- (12) Nakai, M.; Obata, M.; Sekiguchi, F.; Kato, M.; Shiro, M.; Ichimura, A.; Kinoshita, I.; Mikuriya, M.; Inohara, T.; Kawabe, K.; Sakurai, H.; Orvig, C.; Yano, S. J. Inorg. Biochem. **2004**, 98, 105.
- (13) Kodama, S.; Yoshida, J.; Nomoto, A.; Ueta, Y.; Yano, S.; Ueshima, M.; Ogawa, A. *Tetrahedron Lett.* **2010**, *51*, 2450.
- (14) Monopoli, A.; Cotugno, P.; Iannone, F.; Ciminale, F.; Dell'Anna, M. M.; Mastrorilli, P.; Nacci, A. Eur. J. Org. Chem. 2014, 5925.
- (15) (a) Brząszcz, M.; Kloc, K.; Młochowski, J. Pol. J. Chem. 2003, 77, 1579. (b) Chu, G.; Li, C. Org. Biomol. Chem. 2010, 8, 4716. (c) Wu, X.-F.; Petrosyan, A.; Ghochikyan, T. V.; Saghyan, A. S.; Langer, P. Tetrahedron Lett. 2013, 54, 3158.
- (16) Marui, K.; Nomoto, A.; Ueshima, M.; Ogawa, A. *Tetrahedron Lett.* **2015**, *56*, 1200.
- (17) (a) Allen, S. E.; Walvoord, R. R.; Padilla-Salinas, R.; Kozlowski, M.
 C. *Chem. Rev.* 2013, *113*, 6234. (b) Minakata, S.; Ohshima, Y.; Takemiya, A.; Ryu, I.; Komatsu, M.; Ohshiro, Y. *Chem. Lett.* 1997,

- 26, 311. (c) Maeda, Y.; Nishimura, T.; Uemura, S. Bull. Chem. Soc. Jpn. 2003, 76, 2399. (d) Patila, R. D.; Adimurthy, S. Adv. Synth. Catal. 2011, 353, 1695. (e) Largeron, M.; Fleury, M.-B. Angew. Chem. Int. Ed. 2012, 51, 5409. (f) Kang, Q.; Zhang, Y. Green Chem. 2012, 14, 1016. (g) Hu, Z.; Kerton, F. M. Org. Biomol. Chem. 2012, 10, 1618. (h) Lan, Y.-S.; Liao, B.-S.; Liu, Y.-H.; Peng, S.-M.; Liu, S.-T. Eur. J. Org. Chem. 2013, 5160. (i) Huang, B.; Tian, H.; Lin, S.; Xie, M.; Yu, X.; Xu, Q. Tetrahedron Lett. 2013, 54, 2861. (j) Wang, J.; Lu, S.; Cao, X.; Gu, H. Chem. Commun. 2014, 50, 5637. (k) Bai, L; Dang, Z. RSC Adv. 2015, 5, 10341.
- (18) Xiao, T.; Xiong, S.; Xie, Y.; Dong, X.; *Zhou*, *L. RSC Adv.* **2013**, 3, 15592.
- (19) (a) Bailey, A. J.; James, B. R. Chem. Commun. 1996, 2343.
 (b) Yuan, Q. L.; Zhou, X. T.; Ji, H. B. Catal. Commun. 2010, 12, 202.
 (c) Berlicka, A.; König, B. Photochem. Photobiol. Sci. 2010, 9, 1359. (d) Zhou, X. T.; Ren, Q. G.; Ji, H. B. Tetrahedron Lett. 2012, 53, 3369. (e) Zhao, S.; Liu, C.; Guo, Y.; Xiao, J. C.; Chen, Q. Y. J. Org. Chem. 2014, 79, 8926. (f) Ushakov, D. B.; Plutschack, M. B.; Gilmore, K.; Seeberger, P. H. Chem. Eur. J. 2015, 21, 6528.
- (20) (a) Furukawa, S.; Ohno, Y.; Shishido, T.; Teramura, K.; Tanaka, T. ACS Catal. 2011, 1, 1150. (b) Rueping, M.; Vila, C.; Szadkowska, A.; Koenigs, R. M.; Fronert, J. ACS Catal. 2012, 2, 2810. (c) Ko, J. H.; Kang, N.; Park, N.; Shin, H.-W.; Kang, S.; Lee, S. M.; Kim, H. J.; Ahn. T. K.: Son. S. U. ACS Macro Lett. 2015. 4. 669. (d) Su. F.: Mathew, S. C.; Möhlmann, L.; Antonietti, M.; Wang, X.; Blechert, S. Angew. Chem. Int. Ed. 2011, 50, 657. (e) Lang, X.; Ji, H.; Chen, C.; Ma, W.; Zhao, J. Angew. Chem. Int. Ed. 2011, 50, 3934. (f) Suzuki, K.; Tang, F.; Kikukawa, Y.; Yamaguchi, K.; Mizuno, N. Angew. Chem. Int. Ed. 2014, 53, 5356. (g) Yang, X.-J.; Chen, B.; Li, X.-B.; Zheng, L.-Q.; Wu, L.-Z.; Tunga, C.-H. Chem. Commun. 2014, 50, 6664. (h) Lang, X.; Ma, W.; Zhao, Y.; Chen, C.; Ji, H.; Zhao, J. Chem. Eur. J. 2012, 18, 2624. (i) Huang, L.; Zhao, J.; Guo, S.; Zhang, C.; Ma, J. J. Org. Chem. 2013, 78, 5627. (j) Park, J. H.; Ko, K. C.; Kim, E.; Park, N.; Ko, J. H.; Ryu, D. H.; Ahn, T. K.; Lee, J. Y.; Son, S. U. Org. Lett. 2012, 14, 5502. (k) Jin, J.; Shin, H.-W.; Park, J. H.; Park, J. H.; Kim, E.; Ahn, T. K.; Ryu, D. H.; Son, S. U. Organometallics 2013, 32, 3954. (l) Ashen-Garry, D.; Selke, M. Photochem. Photobiol. 2014, 90, 257. (m) Zavahir, S.; Zhu, H. Molecules 2015, 20, 1941. (n) Ohtani, B.; Osaki, H.; Nishimoto, S.-i.; Kagiya, T. Chem. Lett. 1985, 14, 1075. (o) Ho, H.-A.; Manna, K.; Sadow, A. D. Angew. Chem. Int. Ed. 2012, 51, 8607. (p) Li, N.; Lang, X.; Ma, W.; Ji, H.; Chen, C.; Zhao, J. Chem. Commun. 2013, 49, 5034. (q) Naya, S.-i.; Kimura, K.; Tada, H. ACS Catal. 2013, 3, 10.
- (21) Pereiro, A. B.; Tojo, E.; Rodriguez, A.; Canosa, J.; Tojo, J. *Green Chem.* **2006**, 8, 307.
- (22) (a) Rebelo, S. L. H.; Simões, M. M. Q.; Neves, M. G. P. M. S.; Silva, A. M. S.; Tagliatesta, P.; Cavaleiro, J. A. S. J. Mol. Catal. A: Chem. 2005, 232, 135. (b) Kumar, A.; Maji, S.; Dubey, P.; Abhilash, G. J.; Pandey, S.; Sarkar, S. Tetrahedron Lett. 2007, 48, 7287. (c) Hirohara, S.; Obata, M.; Alitomo, H.; Sharyo, K.; Ando, T.; Yano, S.; Tanihara, M. Bioconjugate Chem. 2009, 20, 944. (d) de Souza, J. M.; de Assis, F. F.; Carvalho, C. M. B.; Cavaleiro, J. A. S.; Brocksom, T. J.; de Oliveira, K. T. Tetrahedron Lett. 2014, 55, 1491.