

Award Accounts

The Chemical Society of Japan Award for Young Chemists for 2005

Catalytic Radical Cyclization of Oximes Induced by One-Electron Transfer

Mitsuru Kitamura*[1] and Koichi Narasaka[2]

[1]Department of Applied Chemistry, Faculty of Engineering, Kyushu Institute of Technology, 1-1 Sensui-cho, Tobata-ku, Kitakyushu 804-8550

[2]Division of Chemistry and Biological Chemistry, School of Physical Sciences and Mathematical Sciences, Nanyang Technological University, 1 Nanyang Walk, Block 5, Level 3, Singapore 637616

Received November 2, 2007; E-mail: kita@che.kyutech.ac.jp

Anion radicals generated by one-electron reduction of oxime derivatives act as iminyl radical equivalents. That is, the intramolecular C–N bond formation of γ,δ-unsaturated or β-aryl oximes is induced by one-electron reduction to give various aza-heterocycles. The catalytic electron transfer processes are developed by using hydroquinones or copper reagents as electron donors. Photo-induced electron transfer is also utilized to transform of γ,δ-unsaturated oximes to dihydropyrroles. Total synthesis of peduncularine was achieved by applying the catalytic radical cyclization of oximes as a key step.

1. Introduction

In aza-heterocycle synthesis, iminyl radicals (alkylideneaminyl radicals) have been employed as reactive intermediates,[1] in which oxime derivatives have been used as the radical sources. For example, Forrester et al. reported the synthesis of quinolines by the cyclization of the iminyl radical formed by the oxidation of *O*-(carboxylmethyl)oxime.[2] Zard et al. have studied extensively the generation of iminyl radical species from oximes and their addition reaction to internal alkenes.[3,4] For the generation of iminyl radical species, they have developed various methods; such as the action of nBu$_3$SnH/AIBN on *O*-substituted oxime, the reduction of *O*-acetyloxime with nickel powder, and so on. Weinreb et al. devised an efficient cyclization method for *O*-(2,6-dimethylphenylsulfinyl)oximes by applying the Hudson reaction.[5] Recently, photo-induced iminyl radical cyclization was reported by Rodríguez's group.[6]

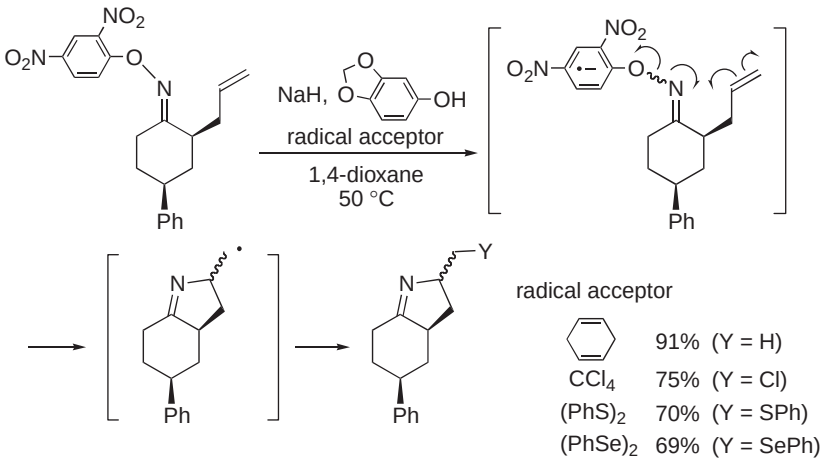
During the course of study on abnormal S_N2-type reaction at sp^2 atoms of oximes,[7] we observed that anion radicals of oxime derivatives acted as alkylideneaminyl radical equivalents, and were utilized as reactive intermediates for C–N bond formation. That is, γ,δ-unsaturated ketone *O*-2,4-dinitrophenyloximes cyclized smoothly to 3,4-dihydro-2*H*-pyrroles by treatment with sodium hydride and 3,4-methylenedioxyphenol (Scheme 1).[8] The reaction was initiated by one electron reduction of the oxime with sodium hydride and 3,4-methylenedioxyphenol to form an anion radical species. Successively, radical cyclization proceeded to form an alkyl radical, which was trapped with a radical trapping reagent such as CCl_4, $(PhS)_2$, or $(PhSe)_2$.

Similar radical cyclizations have been found to proceed by intramolecular electron transfer. By treatment with excess sodium hydride, 3-[3-(2,4-dinitrophenoxyimino)butyl]phenol (**1a**) cyclized to quinoline derivatives **2a** and **3a** (Scheme 2).[9] In this reaction, first a phenoxide–excess NaH complex was formed, from which electron transfer to the dinitrophenyl group in **4** occurred. In the resulting anion radical species **5**, radical coupling between phenoxyl radical and oxime nitrogen proceeded with the elimination of 2,4-dinitrophenoxide affording dihydroquinolinol **6**. Quinolinol **2a** and tetrahydro derivative **3a** were formed by disproportionation of **6**.

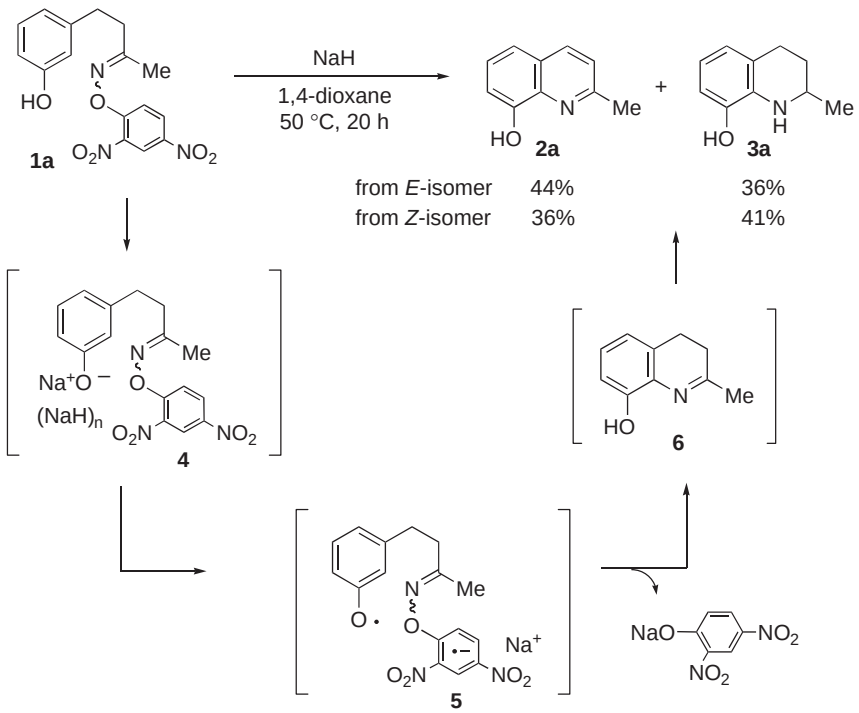
8-Quinolinols **2** were found to be exclusively prepared from 3-[3-(2,4-dinitrophenoxyimino)butyl]phenol **1** by radical cyclization and successive one-pot oxidation with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) and acetic acid (Scheme 3).[9a] In contrast, when the cyclization was carried out with NaH in the presence of a reducing reagent, Na[BH_3CN], tertrahydro-8-quinolinols **3** were obtained (Scheme 3).[10] Both methods exhibited wide generality and various 8-quinolinols and tetrahydro-8-quinolinols were synthesized selectively from β-(3-hydroxyphenyl)oximes. In addition, it was quite noteworthy that both stereoisomers of *O*-(2,4-dinitrophenyl)oximes can be employed in the synthesis of quinolinol derivatives in all cases.[11]

Although it is apparent that one electron reduction of *O*-(2,4-dinitrophenyl)oximes induces radical cyclization to afford azaheterocycles, the reaction has to be performed under strongly basic conditions, and the 2,4-dinitrophenyl group is not a good leaving group in the sense of atom economy and availability of the starting material.

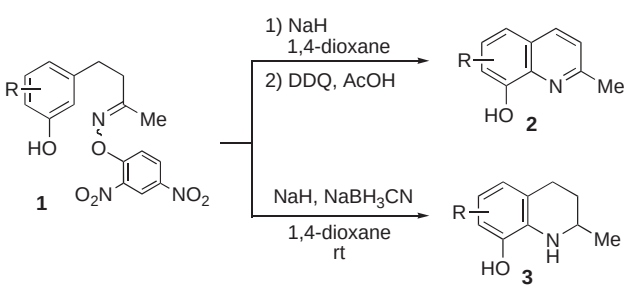
Published on the web May 14, 2008; doi:10.1246/bcsj.81.539



Scheme 1. Radical cyclization of *O*-2,4-dinitrophenyl oxime by intermolecular single electron transfer.

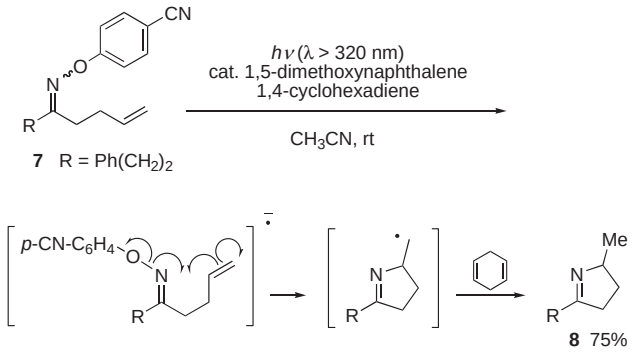


Scheme 2. Radical cyclization of *O*-(2,4-dinitrophenyl)oxime by intramolecular single electron transfer.



Scheme 3. Synthesis of 8-quinolinols and tetrahydro-8-quinolinols.

A photo-induced electron-transfer process was also applied to the radical cyclization of oximes. Photo irradiation ($\lambda > 320$ nm) of a mixture of γ,δ-unsaturated *O*-(*p*-cyanophenyl)oxime **7** and 1,5-dimethoxynaphthalene (DMN) in acetonitrile gave 3,4-dihydro-2*H*-pyrrole **8** (Scheme 4).[12] In this reaction, the exited 1,5-dimethoxynaphthalene was used as a one-electron reductant. To make the electron transfer efficient, a *p*-cyanophenyl group was introduced as a substituent of the oxime oxygen, but it was not easy to prepare the *O*-(*p*-cyanophenyl)oximes. It was desired to replace the *p*-cyanophenyl group with a simple substituent that was more readily available as a starting material.



Scheme 4. Photo-induced radical cyclization of *O*-(*p*-cyanophenyl)oxime **7**.

Accordingly, we started to improve this radical cyclization, and we focused particularly on the development of a catalytic reaction and modification of the leaving group on the oxime nitrogen. In this account is described the catalytic radical cyclization of oximes via anion radicals.

2. Cyclization of *O*-Acetyloximes of γ,δ-Unsaturated Ketones by Photochemical Electron Transfer[13]

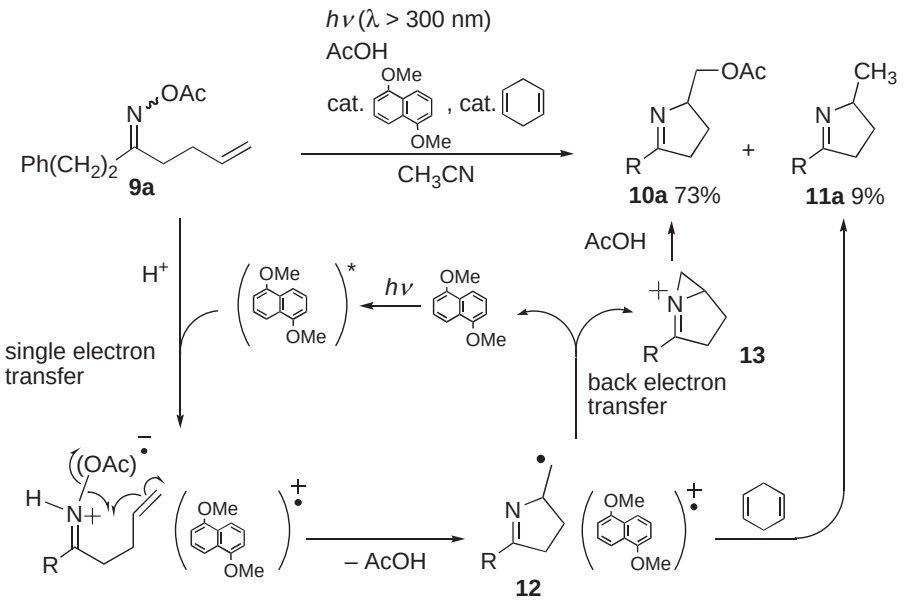
Of course, γ,δ-unsaturated *O*-acetyloxime **9a** is hardly cyclized by photo-induced electron transfer with 1,5-dimethoxynaphthalene (yield of **10a** and **11a** are both 4%), because the *O*-acetyloxime does not act as a good electron acceptor. The addition of acetic acid, however, accelerates the electron transfer, in which the protonated *O*-acetyloxime, generated in equilibrium, might work as a good electron acceptor. That is, in the presence of 10 molar amounts of acetic acid, γ,δ-unsaturated *O*-acetyloxime **9a** cyclized to 4-acetoxymethy-3,4-dihydropyrroles **10a** and **11a** in acetonitrile under photo irradiation ($\lambda > 300$ nm) using 1,5-dimethoxynaphthalene as a catalytic sensitizer (Scheme 5). The addition of a small amount of 1,4-cyclohexadiene (20 mol %) made the reaction cleaner. It presumably acted as a scavenger of some radical species such as those generated from the solvent.

This cyclization is induced by single electron transfer from excited 1,5-dimethoxynaphthalene to protonated oxime **9a** and the cyclization with cleavage of the N–O bond gives alkyl radical species **12**. Back electron transfer from **12** to the cation radical of 1,5-dimethoxynaphthalene regenerates the sensitizer, 1,5-dimethoxynaphthalene, and cationic species **13** is trapped with AcOH immediately to give acetoxymethyl 2*H*-dihydropyrrole **10a**. Methylated dihydropyrrole **11a** is formed from alkyl radical species **12** by abstracting hydrogen from 1,4-cyclohexadiene.

Various γ,δ-unsaturated *O*-acetyloximes of alkyl ketones were converted to dihydropyrroles (Table 1). Cyclization of **9** having a terminal vinyl group gave acetoxymethyl cyclic imine **10** and a small amount of hydrogenated **11** (Runs 1 and 5), while oximes having an internal alkenyl moiety gave acetoxymethyl imines **10** exclusively (Runs 2–4). From γ-substituted γ,δ-unsaturated oxime **11**, pyridine **15** was formed in 15% yield via 6-*endo* cyclization along with a 58% total yield of 5-membered cyclic imines (Run 5).

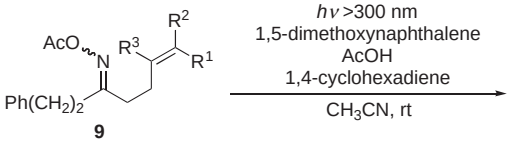
Thus, the cyclization of alkyl ketone *O*-acetyloximes **9** proceeded by photo-sensitized electron transfer in the presence of acetic acid, whereas acetic acid did not show any effect in the cyclization of aryl or conjugated ketone *O*-acyloximes **16** (Table 2). The cyclization of **16** finished within a shorter time as compared to that of non-conjugated oximes **9**, and 2-methyldihydropyrroles **18** were obtained instead of 2-acetoxymethyl derivatives (Runs 1, 3, 5, and 7). Some *O*-methoxyoximes **17** also cyclized under the same conditions (Runs 2, 4, and 6). Because the cyclization proceeded quite slowly in the absence of 1,5-dimethoxynaphthalene, the reaction seemed to be initiated by energy transfer through the exciplex formation between excited 1,5-dimethoxynaphthalene and conjugated oximes.

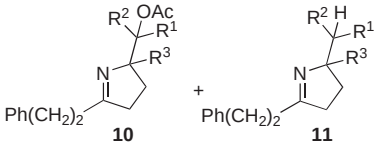
Concerning photochemical radical reaction of oximes, Zard et al. reported an efficient radical chain cyclization of *O*-(methylthio)thiocarbonyloxime initiated by homolytic cleavage of an N–O bond by photo irradiation (Scheme 6).[4c]



Scheme 5. Photo-induced radical cyclization of *O*-acetyloxime **9a**.

Table 1. Photo-Induced Radical Cyclization of *O*-Acetyloximes **9**[a)]





Run	R^1	R^2	R^3	**20**/%	**21**/%
1	H	H	H	73	9
2[b)]	H	Me	H	82[c)]	0
3	H	Ph	H	76[d)]	0
4[e)]	Me	Me	H	80	0
5[f)]	H	H	Me	47	11

a) Oxime:1,5-dimethoxynaphthalene:AcOH:1,4-cyclohexadiene = 1:0.2:10:0.2. b) The stereochemistry of olefin moiety was *E*:*Z* = 10:3. c) Diastereomer mixture (4:1). d) Diastereomer mixture (7:3). e) **14** was obtained in 10% yield. f) **15** was obtained in 15% yield.

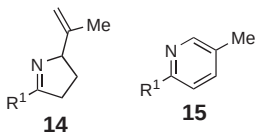
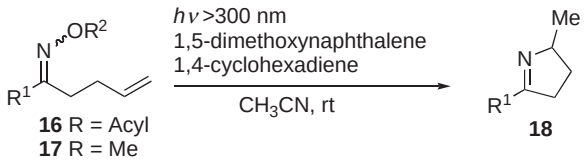
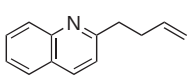


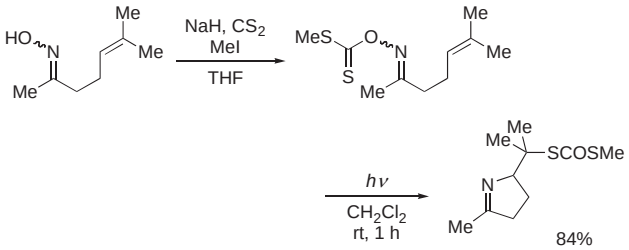
Table 2. Photochemical Cyclization of Conjugated Ketone Oximes[a)]



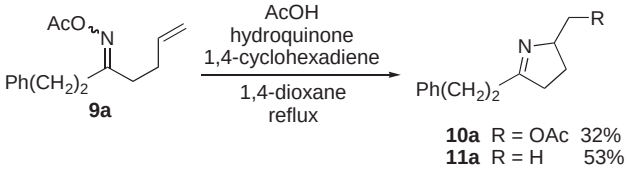
Run	R^1	R^2	*syn*:*anti*	Time/h	Yield/%
1	Ph	Ac	1:0	0.5	77
2		Me	1:0	3	79
3	Ph(CH2)3OC(=O)–	*t*-BuC(O)–	1:0	2	56
4		Me	1:0	5	53
5	Ph	Ac	3:7	2	12
6		Me	3:5	9	56
7[b)]	Ph	Ac	3:8	5	63
8[b)]		Me	6:11	20	0

a) Oxime:1,5-dimethoxynaphthalene:1,4-cyclohexadiene = 1:0.2:10. b) **19** was obtained (Run 7: 12% and Run 8: 5%).





Scheme 6. Photochemical radical reaction of *O*-(methylthio)thiocarbonyloxime.



Scheme 7. Hydroquinone-catalyzed cyclization of *O*-acetyloxime **9a**.

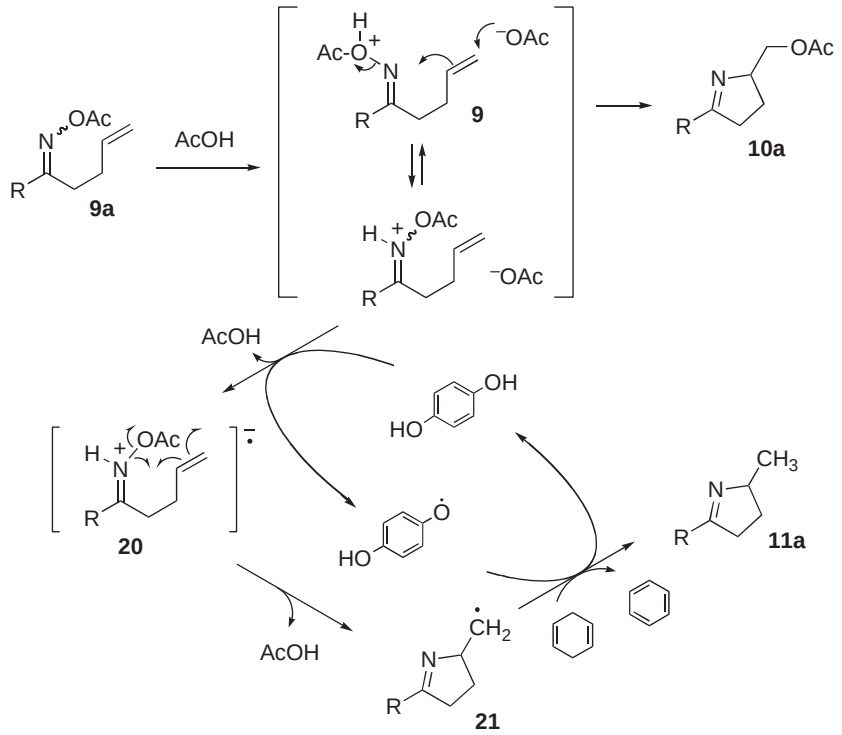
3. Hydroquinone-Catalyzed Cyclization of *O*-Acetyloximes of γ,δ-Unsaturated Ketones[14]

In addition to photochemical one electron reduction, catalytic radical cyclizations of γ,δ-unsaturated *O*-acetyloxime were explored by employing electron-donor catalysts. In the first example, dihydroquinone (or 1,5-naphthalenediol) was found to catalyze the cyclization with the coexistence of acetic acid. When a 1,4-dioxane solution of γ,δ-unsaturated *O*-acetyloxime **9a**, acetic acid, 1,4-cyclohexadiene, and a catalytic amount of hydroquinone was heated, methyldihydropyrrole **11a** was obtained in 53% yield along with acetoxymethyl derivative **10a** (Scheme 7).

A plausible mechanism for the formation of **10a** and **11a** is shown in the Scheme 8. **11a** would be formed by radical cyclization. One-electron transfer occurs from hydroquinone to the protonated *O*-acetyloxime **9**, and the resulting protonated anion radical **20** cyclizes to generate alkyl radical **21**, which abstracts hydrogen from 1,4-cyclohexadiene to afford **11a**. The catalyst, hydroquinone, is regenerated from phenoxyl radical by hydrogen abstraction from 1,4-cyclohexadiene. On the other hand, **10a** would be formed by S_N2-type substitution on the oxime nitrogen.[15]

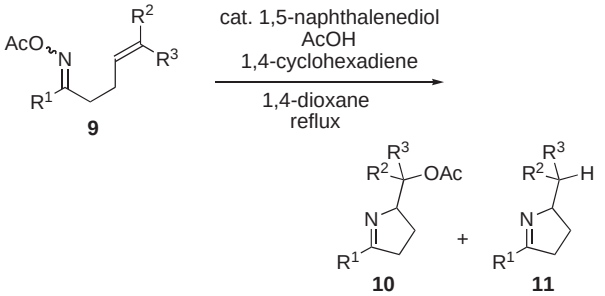
In the reaction of *O*-acetyloxime **9** having an electron-rich olefinic moiety, the olefinic moiety acted as a nucleophile and acetoxymethyl derivative **10** was obtained as a major product by S_N2-type cyclization (Table 3, Runs 2 and 3). In contrast, only radical cyclization products **11** were obtained from oximes **9** which had an electron-deficient olefinic moiety (Runs 4 and 5). *O*-Acyloximes of phenyl ketone and α-keto ester also cyclized to give only radical cyclization products, dihydropyrroles **11** (Runs 6 and 7).

This method could be applied to the preparation of pyrroles from β-alkynyl ketone *O*-acetyloximes having an alkynyl moiety as shown in Table 4. Both alkyl and aryl ketoximes **22** having a terminal alkynyl group were converted to 2,5-disubstituted pyrroles **23** in good yields irrespective of the terminal substituent on the alkynyl group.



Scheme 8. Plausible reaction mechanism of the formation of **10a** and **11a**.

Table 3. Cyclization of *O*-Acetyloximes **9** Catalyzed by 1,5-Naphthalenediol[a)]



Run	R^1	R^2	R^3	*syn*:*anti*	Time/h	**10**/%	**11**/%
1	$Ph(CH_2)_2$	H	H	1:1	6	34	52
2[b)]	$Ph(CH_2)_2$	Me	H	1:1	6	67[c)]	16
3	$Ph(CH_2)_2$	Me	Me	1:1	6	72	5
4	$Ph(CH_2)_2$	CN	H	1:1	12	0	69
5	$Ph(CH_2)_2$	CO_2Et	H	1:2	12	0	72
6	Ph	H	H	>99:<1	8	0	75
7[d)]	$Ph(CH_2)_2O_2C$	H	H	>99:<1	6	0	67

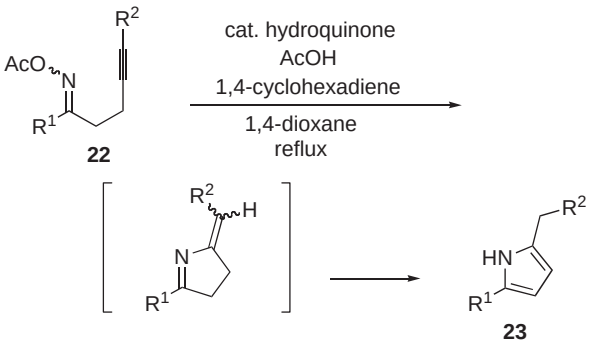
a) Oxime:1,5-naphthalenediol:acetic acid:1,4-cyclohexadiene = 1:0.05:2.0:10. b) The stereochemistry of olefin moiety was *E*:*Z* = 5:1. c) Diastereomer mixture (2:1). d) *O*-Pivaloyloxime was used instead of *O*-acetyloxime.

4. Cyclization of *O*-Acyloximes of γ,δ-Unsaturated or β-Indolyl Ketones with Copper-Catalysts

It was expected that oxime derivatives would be reduced with low-valent transition-metal compounds. Such an example was reported by Zard et al.: The treatment of γ,δ-unsaturated *O*-acetyloximes with nickel powder and acetic acid in 2-propanol leads to cyclization to dihydropyrroles.[3c] The reaction, however, requires a large excess of nickel powder, and it would be desirable to conduct such a transformation in a catalytic manner.

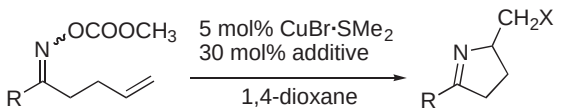
Copper(I) complexes were found to work as redox catalysts.[16] When a *syn*/*anti* (1:1) mixture[11] of the *O*-methoxycarbonyloxime of γ,δ-unsaturated ketone **24** and 5 mol % of $CuBr\cdot SMe_2$ in 1,4-dioxane was heated to 80 °C, cyclic imine **11a** was obtained in 39% yield (Scheme 9). The product yield was improved by the addition of LiBr, and 4-(bromomethyl)-3,4-dihydropyrrole **25a** was obtained in 86%. As well as *O*-

Table 4. Cyclization of Alkynyl Ketone *O*-Acetyloximes **22** Catalyzed by Hydroquinone[a)]



Run	R^1	R^2	Time/h	Yield/%
1	$PhCH_2CH_2$[b)]	H	24	67
2	Ph[c)]	H	24	67
3	Ph[c)]	Me	24	72
4	Ph[c)]	CO_2Et	28	83
5	Me[d)]	Ph	6	32

a) Oxime **22**:hydroquinone:acetic acid:1,4-cyclohexadiene = 1:0.05:2.0:10. b) *syn*:*anti* = 1:1. c) Only *syn*-isomer was used. d) Only *anti*-isomer was used.



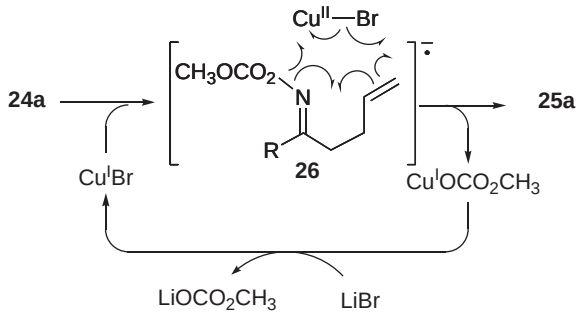
additive	product	Yield/%
none	**11a** (X = H)	39
LiBr	**25a** (X = Br)	86

Scheme 9. Copper-catalyzed cyclization of *O*-methoxycarbonyloxime **24a**.

methoxycarbonyloxime, *O*-pentafluorobenzoyloxime was cyclized in high yield, whereas the corresponding *O*-2,4-dinitrophenyl and *O*-acetyloximes were not appropriate for this catalytic system. This reaction probably proceeds by electron transfer from copper(I) salt to the oxime **24a**, generating anion radical, which in turn cyclizes to give **25a** with the elimination of Cu^I (Scheme 10).

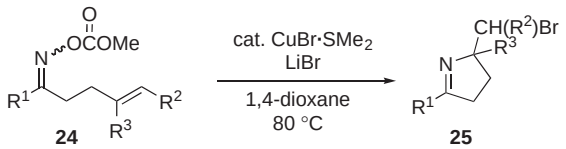
The catalytic process with $CuBr \cdot SMe_2$–LiBr could be applied to the cyclization of various γ,δ-unsaturated ketone *O*-methoxycarbonyloximes as shown in Table 5. Cyclization of oximes having a γ-substituted alkenyl moiety gave cyclic imines in high yield (Runs 1 and 2). From δ-methyl-substituted oxime, 5,5-disubstituted dihydropyrrole was obtained in 53% yield along with 16% yield of disubstituted pyridine **15** (Run 3). Phenyl ketone and α-keto ester oximes were smoothly transformed into 2-phenyl- and 2-ethoxycarbonyldihydropyrroles, respectively (Runs 4 and 5).

Furthermore, α-carbolines **28** were prepared by radical cyclization of β-(3-indolyl) ketone *O*-pentafluorobenzoyloximes **27** with a catalytic amount of copper powder in 1,2-dichloroethane and by successive oxidation with chloranil (Table 6).[17]



Scheme 10. Plausible mechanism of copper-catalyzed cyclization.

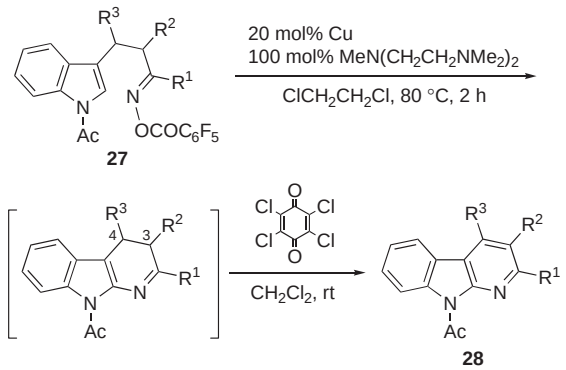
Table 5. Cu-Catalyzed Cyclization of *O*-Methoxycarbonyloximes **24**



Run	R^1	R^2	R^3	*syn*:*anti*	Yield/%
1	$Ph(CH_2)_2$	Me	H	1:1	85
2	$Ph(CH_2)_2$	Ph	H	1:1	74
3[a)]	$Ph(CH_2)_2$	H	Me	1:1	53
4	Ph	H	H	>99:<1	83
5	CO_2Et	H	H	>99:<1	53

a) **15** was obtained in 16% yield.

Table 6. Synthesis of α-Carbolines **28**

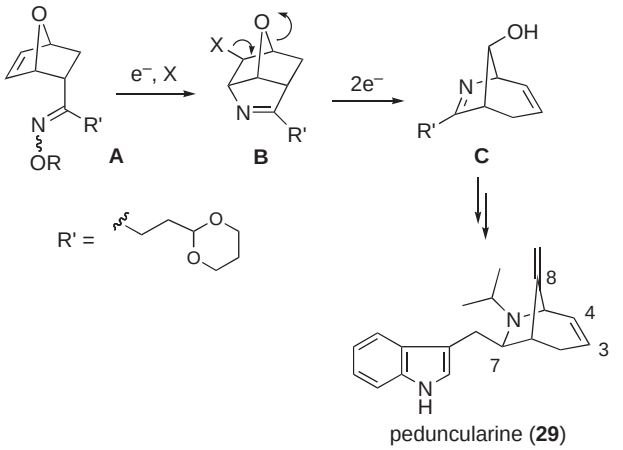


R^1	R^2	R^3	Yield/%
Me	H	H	75
Me	Me	H	83
Me	H	CO_2t-Bu	67
	$-(CH_2)_4-$	H	39

In this radical cyclization, copper powder gradually reacted with 1,2-dichloroethane to generate copper(I) salt, which acted as an active redox catalyst for the anion radical generation.

5. Total Synthesis of Peduncularine[18]

Peduncularine (**29**) was isolated from the Tasmanian shrub *Aristoteria peduncularis* in 1971 by Bick and co-workers[19] and the structure was determined in 1979.[20] Peduncularine consists of an unusual 6-azabicyclo[3.2.1]octene core with a



Scheme 11. Synthetic plan for peduncularine (**29**).

3-indolylmethyl group and is reported to show cytotoxic activity against breast cancer cell lines.[21] The unique structure coupled with the biological activity makes this compound an attractive synthetic target.[22]

We were interested in the synthesis of peduncularine by employing the radical cyclization of oximes as a key step to construct the 6-azabicyclo[3.2.1]octene framework, and started the synthetic study of peduncularine. Our synthetic plan for peduncularine (**29**) is shown in Scheme 11. 6-Azabicyclo-[3.2.1]octene **C** would be synthesized by the radical cyclization of oxime **A** having a 7-oxabicyclo[2.2.1]heptene moiety, followed by reductive ring opening of the resulting tricyclic imine **B**.

Radical cyclization of *O*-(2,4-dinitrophenyl)oxime **30a** proceeded smoothly by treatment with NaH and 3,4-methylenedioxyphenol (sesamol) in the presence of diphenyl diselenide at 50 °C for 2 h, and the expected tricyclic imine *exo*-**31a** possessing a phenylseleno group was obtained in 77% yield (Table 7, Run 1). The product yield was increased to 93% when the reaction was carried out at room temperature for 24 h (Run 2). *O*-Methoxycarbonyloxime **30b** was cyclized slowly to form bromotricyclic imine **31b** in moderate yield (65%, *exo*:*endo* = 1:3) by treatment with an equimolar amount of $CuBr \cdot SMe_2$ (Run 3). A stoichiometric and a catalytic cyclization of pentafluorobenzoyloxime **30c** with $CuBr \cdot SMe_2$ proceeded smoothly to afford imine **31b** in 98% yield (Run 4) and 75% yield (Run 5), respectively. In the case of the Cu-mediated reaction, the *endo* isomer was formed as a major product.

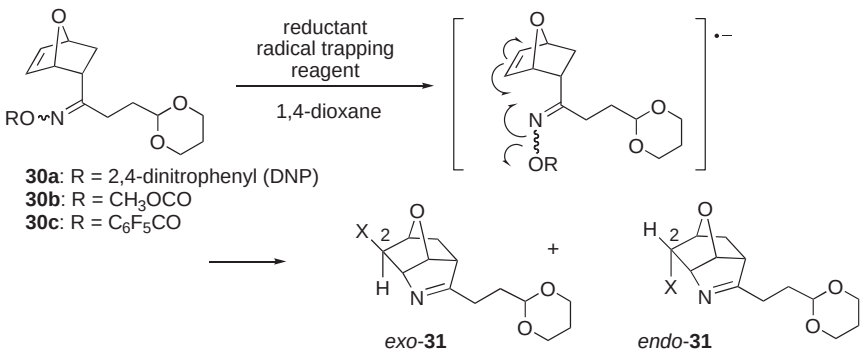
Reductive ring opening of **31a** and **31b** proceeded by treatment with lithium naphthalenide, giving the desired 6-azabicyclooctene **32** (Scheme 12). Because imine **32** was found to be easily hydrolyzed, the crude **32** was converted to *N*-Alloc-enamine **33** with allyloxycarbonyl chloride (AllocCl) and pyridine, which was obtained as a single stereoisomer and was stable enough for chromatographic purification. As expected, construction of the 6-azabicyclo[3.2.1]octene skeleton was successfully achieved by radical cyclization of oximes **30** and the successive reductive ring opening.

A trimethylsilylmethyl group was introduced at position C-8 of **33**, because it would be readily transformed into a methylene group by Peterson olefination. Alcohol **33** was oxidized and the resulting ketone was treated with triethylsilylmethyl Grignard reagent to give the corresponding alcohol **34**. Due to the silylmethyl group, the ene carbamate portion of **34** was reduced face selectively and the alkene moiety was introduced by Peterson olefination to afford carbamate **35**. Removal of the allyloxycarbonyl group and introduction of an isopropyl group on nitrogen proceeded smoothly to give cyclic amine **36** which was an intermediate in the total synthesis reported by Klaver, Hiemstra, and Speckamp.[22a] Finally after transformation of the acetal to an indolyl group by the Fischer method, total synthesis of peduncularine (**29**) was achieved.

Conclusion

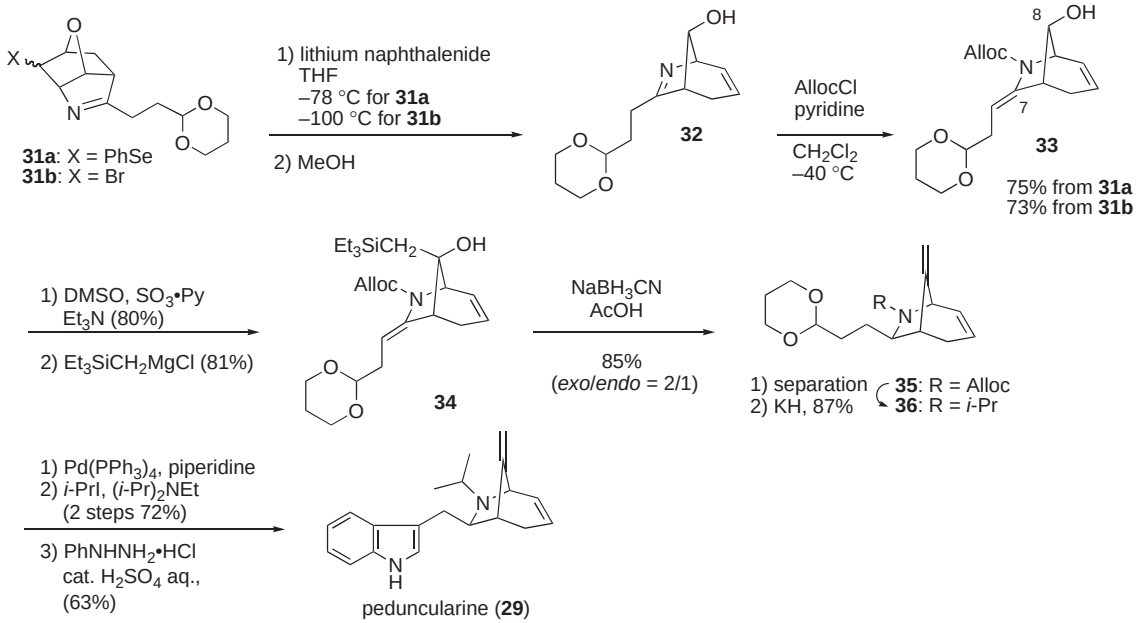
In summary we have developed a catalytic radical cyclization of oximes, and this reaction did not require special technique to treat substrates and reagents. Oximes are easily prepared from the corresponding carbonyl compounds and hy-

Table 7. Radical Cyclization of Oximes **30a–30c**



Run	R		Reagents	Temp/°C	Time/h	X	31	Yield/% (*exo*:*endo*)
1	2,4-DNP[a)]	**30a**	sesamol, NaH, $(PhSe)_2$	50	2	PhSe	**31a**	77 (>99:<1)
2	2,4-DNP[a)]	**30a**	sesamol, NaH, $(PhSe)_2$	rt	24	PhSe	**31a**	93 (>99:<1)
3	CH_3OCO	**30b**	$CuBr \cdot SMe_2$ (1.0), LiBr (4.0)	rt	56	Br	**31b**	65 (1:3)
4	C_6F_5CO	**30c**	$CuBr \cdot SMe_2$ (1.0), LiBr (4.0)	rt	2	Br	**31b**	98 (1:2.2)
5	C_6F_5CO	**30c**	$CuBr \cdot SMe_2$ (0.2), LiBr (4.0)	40	2	Br	**31b**	75 (1:6.5)

a) 2,4-DNP: 2,4-dinitrophenyl.



Scheme 12. Total synthesis of peduncularine (**29**).

droxylamine and are stable to hydrolysis as compared with the corresponding imines. We hope this reaction will be an aid in the synthesis of aza-heterocycles.

References

1 a) A. G. Fallis, I. M. Brinza, *Tetrahedron* **1997**, *53*, 17543. b) T. Mikami, K. Narasaka, in *Advances in Free Radical Chemistry*, ed. by S. Z. Zard, JAI, Stamford, **1999**, Vol. 2, p. 45. c) L. Stella, in *Radicals in Organic Synthesis*, ed. by P. Renaud, M. P. Sibi, Wiley-VCH, Weinheim, **2001**, Vol. 2, p. 407.

2 a) A. R. Forrester, M. Gill, J. S. Sadd, R. H. Thomson, *J. Chem. Soc., Perkin Trans. 1* **1979**, 612. b) S. Atmaram, A. R. Forrester, M. Gill, R. H. Thomson, *J. Chem. Soc., Perkin Trans. 1* **1981**, 1721.

3 a) J. Boivin, A.-C. Callier-Dublanchet, B. Quiclet-Sire, A.-M. Schiano, S. Z. Zard, *Tetrahedron* **1995**, *51*, 6517. b) S. Z. Zard, *Synlett* **1996**, 1148. c) J. Boivin, A.-M. Schiano, S. Z. Zard, H. Zhang, *Tetrahedron Lett.* **1999**, *40*, 4531.

4 a) J. Boivin, E. Fouquet, S. Z. Zard, *Tetrahedron Lett.* **1991**, *32*, 4299. b) M. C. Fong, C. H. Schiesser, *Tetrahedron Lett.* **1993**, *34*, 4347. c) J. Boivin, E. Fouquet, A.-M. Schiano, S. Z. Zard, *Tetrahedron* **1994**, *50*, 1769. d) F. Gagosz, S. Z. Zard, *Synlett* **1999**, 1978.

5 a) X. Lin, D. Stien, S. M. Weinreb, *Org. Lett.* **1999**, *1*, 637. b) X. Lin, G. D. Artman, III, D. Stien, S. M. Weinreb, *Tetrahedron* **2001**, *57*, 8779.

6 R. Alonso, P. J. Campos, B. García, M. A. Rodríguez, *Org. Lett.* **2006**, *8*, 3521.

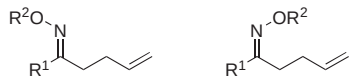
7 a) H. Kusama, Y. Yamashita, K. Narasaka, *Chem. Lett.* **1995**, 5. b) H. Kusama, K. Uchiyama, Y. Yamashita, K. Narasaka, *Chem. Lett.* **1995**, 715. c) H. Kusama, Y. Yamashita, K. Uchiyama, K. Narasaka, *Bull. Chem. Soc. Jpn.* **1997**, *70*, 965. d) S. Mori, K. Uchiyama, Y. Hayashi, K. Narasaka, E. Nakamura, *Chem. Lett.* **1998**, 111. e) K. Uchiyama, M. Yoshida, Y. Hayashi, K. Narasaka, *Chem. Lett.* **1998**, 607. f) M. Yoshida, K. Uchiyama, K. Narasaka, *Heterocycles* **2000**, *52*, 681. g) K. Tanaka, Y. Mori, K. Narasaka, *Chem. Lett.* **2004**, *33*, 26.

8 a) K. Uchiyama, Y. Hayashi, K. Narasaka, *Chem. Lett.* **1998**, 1261. b) K. Uchiyama, Y. Hayashi, K. Narasaka, *Tetrahedron* **1999**, *55*, 8915.

9 a) K. Uchiyama, Y. Hayashi, K. Narasaka, *Synlett* **1997**, 445. b) K. Uchiyama, A. Ono, Y. Hayashi, K. Narasaka, *Bull. Chem. Soc. Jpn.* **1998**, *71*, 2945.

10 A. Ono, K. Uchiyama, Y. Hayashi, K. Narasaka, *Chem. Lett.* **1998**, 437.

11 In this manuscript, the words "*syn*" and "*anti*" are used for the geometry of oximes. *syn* Isomers mean oximes having a leaving group on the oxime nitrogen and a nucleophile or olefin on the same side of the oxime carbon–nitrogen double bond and *anti* isomers mean the opposite as shown below.



12 a) T. Mikami, K. Narasaka, *Chem. Lett.* **2000**, 338. b) T. Mikami, K. Narasaka, *C.R. Acad. Sci., Ser. IIc: Chim.* **2001**, *4*, 477.

13 M. Kitamura, Y. Mori, K. Narasaka, *Tetrahedron Lett.* **2005**, *46*, 2373.

14 a) M. Yoshida, M. Kitamura, K. Narasaka, *Chem. Lett.* **2002**, 144. b) M. Yoshida, M. Kitamura, K. Narasaka, *Bull. Chem. Soc. Jpn.* **2003**, *76*, 2003.

15 M. Kitamura, M. Yoshida, T. Kikuchi, K. Narasaka, *Synthesis* **2003**, 2415.

16 Y. Koganemaru, M. Kitamura, K. Narasaka, *Chem. Lett.* **2002**, 784.

17 K. Tanaka, M. Kitamura, K. Narasaka, *Bull. Chem. Soc. Jpn.* **2005**, *78*, 1659.

18 M. Kitamura, Y. Ihara, K. Uera, K. Narasaka, *Bull. Chem. Soc. Jpn.* **2006**, *79*, 1552.

19 I. R. C. Bick, J. B. Bremner, N. W. Preston, I. C. Calder, *J. Chem. Soc. D* **1971**, 1155.

20 H.-P. Ros, R. Kyburz, N. W. Preston, R. T. Gallagher, I. R. C. Bick, M. Hesse, *Helv. Chim. Acta* **1979**, *62*, 481.

21 I. R. C. Bick, M. A. Hai, in *The Alkaloids*, ed. by A. Brossi,

Academic, New York, **1985**, Vol. 24, p. 113.
22 a) W. J. Klaver, H. Hiemstra, W. N. Speckamp, *J. Am. Chem. Soc.* **1989**, *111*, 2588. b) J. H. Rigby, J. H. Meyer, *Synlett* **1999**, 860. c) X. Lin, D. Stien, S. M. Weinreb, *Tetrahedron Lett.* **2000**, *41*, 2333. d) C. W. Roberson, K. A. Woerpel, *J. Am. Chem. Soc.* **2002**, *124*, 11342. e) D. G. Washburn, R. W. Heidebrecht, Jr., S. F. Martin, *Org. Lett.* **2003**, *5*, 3523.

Award recipient

Mitsuru Kitamura was born in Takamatsu, Japan, in 1971 and received his B.Sc. in 1994 and M.Sc. in 1996 from Keio University. After receiving his Ph.D. in 1999 from Tokyo Institute of Technology under the guidance of Prof. K. Suzuki, he was appointed as a research associate to Prof. Narasaka's group at the University of Tokyo, where he became a lecturer in 2004. In 2005, he moved to Kyusyu Institute of technology as an associate professor. He received the Inoue Research Award for Young Scientists (2000), a Toray Award of the Synthetic Organic Chemical Society (2001), and the CSJ Award for Young Chemists (2005). His research interests are the synthesis of nitrogen heterocycles and the total synthesis of natural products.

Koichi Narasaka was born in Miyagi, Japan, in 1944 and received his B.Sc. in 1967 from Tokyo Institute of Technology. He received his Ph.D. in 1972 under the guidance of Prof. T. Mukaiyama. He became a research associate of the same group in 1972, and then in 1975, moved with Prof. Mukaiyama to the University of Tokyo, where he became a lecturer. His post-doctoral work was with Prof. E. J. Corey at Harvard University from 1975 to 1976. He was appointed to the position of associate professor in 1978, and promoted to a professor in 1987. In 2007, he moved to Nanyang Technological University as a professor. He received the Chemical Society of Japan Award (2000), Louis Pasteur Medal (France, 2001), Merck Schuchardt-Lectureship (Germany, 2002), IAP Lectureship (Columbia University, USA, 2002), Boehringer Ingelheim Lecture Award (University of Toronto, Canada, 2003), and Torey Science and Technology Prize (2004). His research interests are in the area of development of new methods of organic synthesis.