Amination with Oximes

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Keywords: Oxime / S_N2 reaction / Electrophilic amination / Radical cyclization / Iminyl radical / Amino-Heck reaction

The S_N2 reaction has been well recognized not to occur at sp^2 carbons, while such an S_N2-type substitution reaction was found to proceed readily at the sp^2 nitrogen of oximes. Ab initio MP2 calculations show that the activation energy of the nucleophilic substitution at sp^2 nitrogen is almost same as that of the Beckmann rearrangement. By the intramolecular S_N2-type reaction at the oxime nitrogen, various aza-arenes and cyclic imines, such as quinolines, aza-spiro compounds, and dihydropyrroles, can be synthesized. Intermolecular substitution of oximes with organometallic reagents also proceeds, and electrophilic amination of Grignard reagents is accomplished by the use of 4,4,5,5-tetramethyl-1,3-dioxolan-2-one *O*-(phenylsulfonyl)oxime. 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 a single electron transfer to give various pyrroles, quinolines, and carbolines, in which phenols, hydroquinones, or copper reagents can be used as electron donors. A photoinduced radical process is also applied to the transformation of γ,δ-unsaturated oximes to dihydropyrroles. Oxidative addition of oximes to palladium(0) complexes generates alkylideneaminopalladium(II) species, which are utilized as key intermediates in carbon–nitrogen bond formation. Various aza-heterocycles, including pyrroles, pyridines, isoquinolines, spiroimines, and aza-azulenes, are synthesized from *O*-(pentafluorobenzoyl)oximes having olefinic moieties via the intramolecular Heck-type reaction (amino-Heck reaction) by treatment with a catalytic amount of a Pd^0 complex.

Introduction

Oximes are easily prepared from the corresponding carbonyl compounds and hydroxylamine, and are stable to hydrolysis compared with the corresponding imines.[1] Thus, the electrophilicity of the imino carbon of oximes is lower, and addition of nucleophiles to *O*-substituted oximes does not proceed smoothly.

Unsymmetrical oximes have two stereoisomers, i.e. *syn* and *anti* isomers. In some reactions of oximes, the stereochemical feature shows significant influences. Various reactions of oximes have been developed, of which the Beckmann rearrangement is most frequently employed in organic synthesis.[2] In this rearrangement reaction, a C–N

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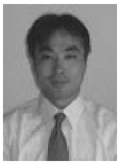

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MICROREVIEWS: This feature introduces the readers to the authors' research through a concise overview of the selected topic. Reference to important work from others in the field is included.

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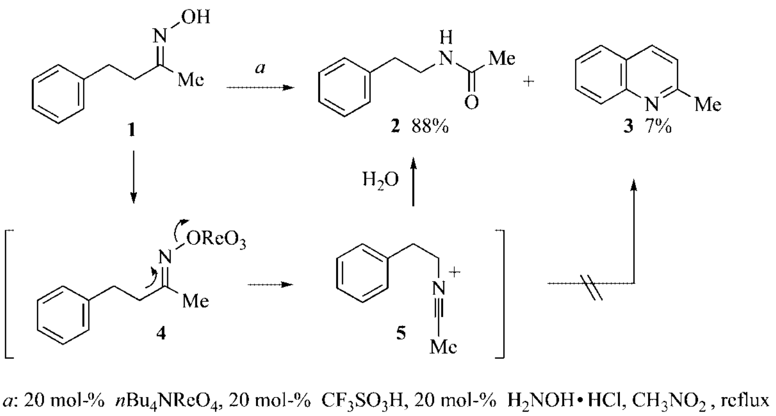
DOI: 10.1002/ejoc.200500389



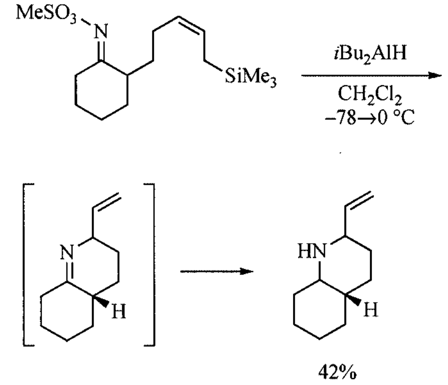
Scheme 1.

bond is newly formed with the migration of the *anti* substituent and the resulting *N*-substituted nitrilium ion intermediates have been widely exploited as synthetic intermediates, not only for amide formation but also for preparation of aza-heterocycles. In addition to the Beckmann rearrangement, there have been some C–N bond forming reactions at the oxime nitrogen atom (vide infra), nevertheless these reactions have not been well generalized as synthetic tools. In this review we describe some C–N bond forming reactions using oximes that have been developed mainly in our laboratory.[3]

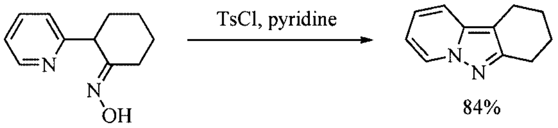
S_N2-Type Substitution

During the course of study on the catalytic Beckmann rearrangement of oximes with tetrabutylammonium perrhenate (nBu$_4$NReO$_4$) and trifluoromethanesulfonic acid (TfOH),[4] we happened to encounter an unexpected phenomenon. That is, by the treatment of 4-phenyl-2-butanone oxime (**1**) with nBu$_4$NReO$_4$ and TfOH, a small amount of 2-methylqunoline **3** was obtained in addition to the expected Beckmann rearrangement product **2** (Scheme 1).[5] Of course, quinoline **3** was not formed via a nitrilium ion intermediate **5** of the Beckmann rearrangement, which should be transformed to 1-methylisoquinoline. The quinoline might have been formed by the cyclization between an oxime nitrogen and a phenyl group.

There are few reports concerning the C–N bond formation at the oxime nitrogen. The cyclization of *O*-sulfonyloximes having an internal allylsilane moiety was reported, while the generality and the mechanism of this reaction have not been studied [Equation (1)].[6] On the other hand, there were some reports on N–N and S–N bond formations at the oxime nitrogen.[7] For example, an internal N–N bond formation proceeded from the *anti*-isomer of α-2-pyridyl oxime by treatment with TsCl and pyridine, whereas the *syn*-isomer could not be cyclized [Equation (2)].

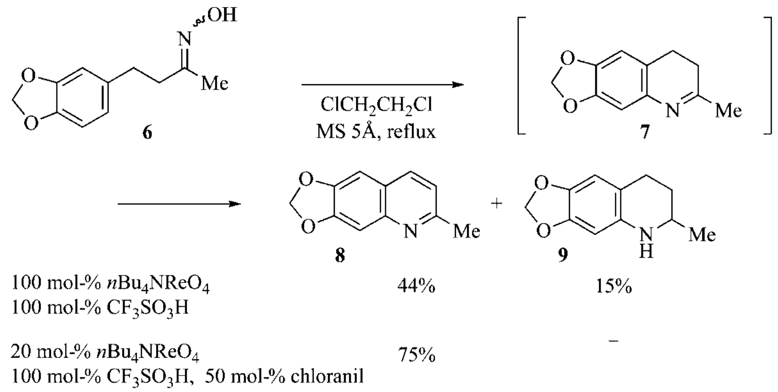


(1)

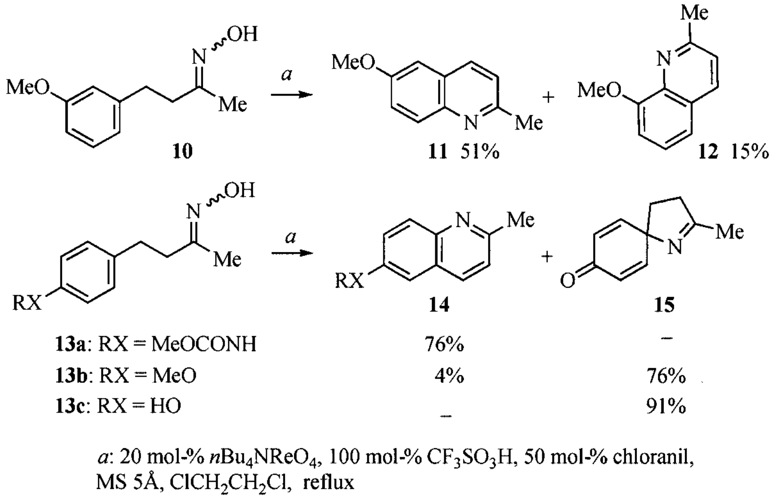


(2)

Accordingly, we were interested in the quinoline formation from phenethyl ketone oxime with nBu$_4$NReO$_4$–TfOH and tried to generalize this cyclization reaction. The reaction course of either the Beckmann reaction or the cyclization was greatly influenced by solvents. That is, in a polar solvent such as nitromethane, the reaction gave the Beckmann rearrangement product **2** preferentially as mentioned in Scheme 1, while quinoline derivatives were obtained in non-polar solvents such as 1,2-dichloroethane without forming the Beckmann product (Scheme 2). The total yield of the cyclization products, quinoline **8** and tetrahydroquinoline **9**, was not good even by using an equimolar amount of nBu$_4$ReO$_4$. Because the higher-valent perrhenate was thought to be consumed in the oxidation of the initially-formed 3,4-dihydroquinoline **7** to quinoline **8**, the reaction was carried out in the presence of tetrachloro-1,4-benzoquinone (chloranil) as an oxidant. The quinoline **8** was obtained in 75% yield without forming tetrahydroquinoline **7**, even with the use of 20 mol-% of nBu$_4$ReO$_4$.



Scheme 2.



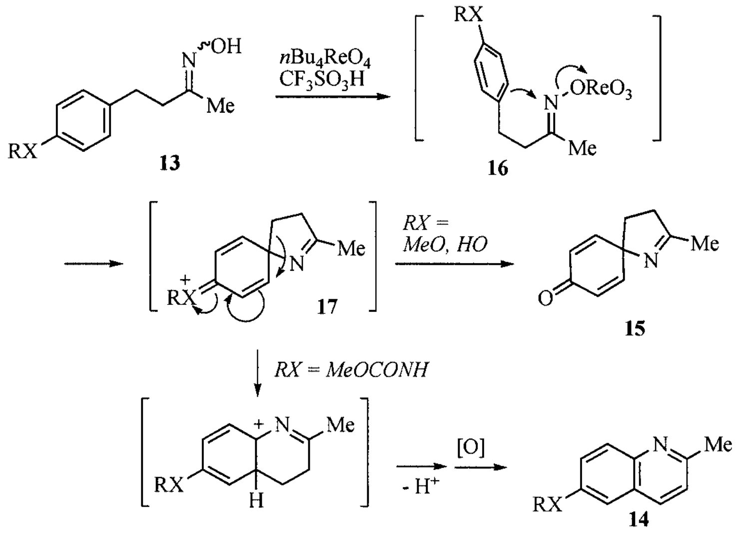
Scheme 3.

As listed in Scheme 3, β-aryl ketone oximes were transformed to aza-heterocycles under Re-catalyzed conditions. From *meta*-methoxy derivative **10**, quinolines were formed as *ortho* and *para* cyclization products. The reaction of *para*-(methoxycarbonylamino)phenethyl ketone oxime **13a** gave 6-substituted quinoline **14** without forming the 7-substituted isomer, while *para*-methoxy or hydroxy derivative **13b** or **13c** cyclized to yield aza-spirotrienones **15**.

These results suggested the course of the cyclization, although the mechanism was not obvious (Scheme 4). In the *para*-substituted oximes, the cyclization occurred initially at the *ipso* position, giving a cationic spirointermediate **17**. When the R–X bond was easily cleaved under the reaction conditions, an aza-spirotrienone was formed, whereas a quinoline was formed via a cyclohexadienone–phenol rearrangement when the R–X bond was hard to cleave.[8] In contrast, the *meta*-substituted oxime seemed to cyclize directly at the *para* and *ortho* positions without forming a spiro intermediate, because 5- and 7-methoxyquinolines, which should be formed from the *ipso*-cyclized intermediate, were not detected at all.

After some experimental and theoretical studies, this cyclizaion was concluded to proceed via a unique S$_N$2-type substitution reaction at the sp^2 nitrogen of oximes, although the S$_N$2 reaction is well recognized not to occur at sp^2 carbons.[9] That is, oxime **13** was converted to perrhenic acid ester **16** and an in-plane nucleophilic attack of the phenyl group occurred at the sp^2 nitrogen atom (Scheme 4). Ab initio MP2 calculations indicated that the activation energies toward the nucleophilic substitution and the Beckmann rearrangement are almost the same, as shown in Figure 1.[10a]

This S$_N$2-type reaction at the oxime sp^2 nitrogen proceeded in general. Five-membered cyclic imine **20** was prepared by treatment of the *anti* isomer of *O*-methylsulfonyl oxime (*E*)-**18**, having an intramolecular active methine group, with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) [Equation (3)].[10b–10c,11] Of course, due to the stereospecificity of S$_N$2-type reaction (in-plane backside attack of nucleophiles relative to leaving groups), *anti O*-sulfonyl oxime (*E*)-**18** was converted smoothly to cyclic imine **20**, whereas the *syn*-isomer (*Z*)-**18** did not cyclize at all.



Scheme 4.

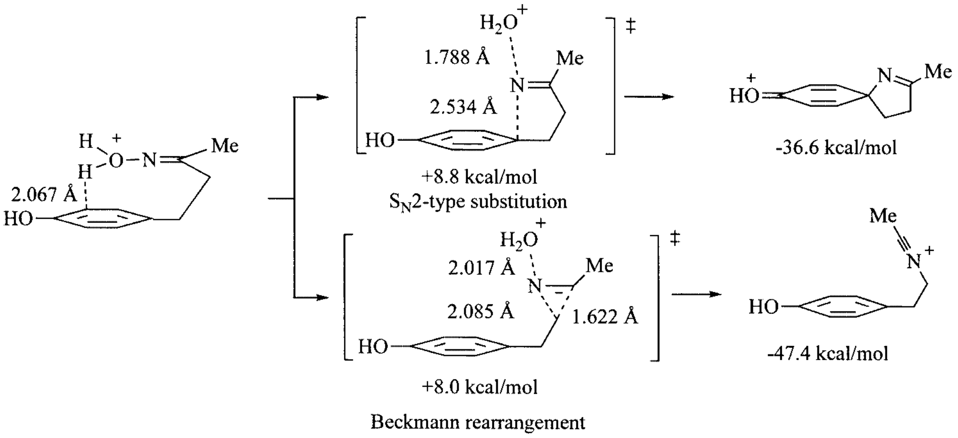
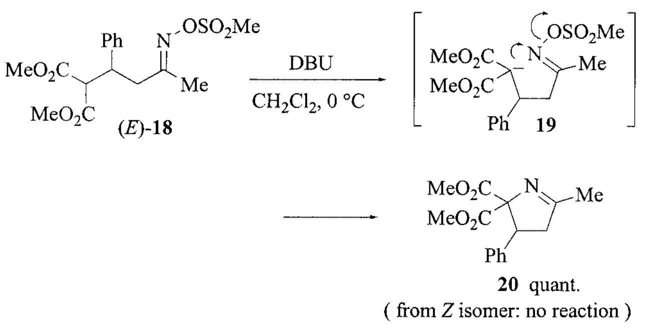


Figure 1. Representative stationary points in the reaction of (*E*)-4-(4-hydroxyphenyl)butan-2-one oxime (MP2/6-31G*).



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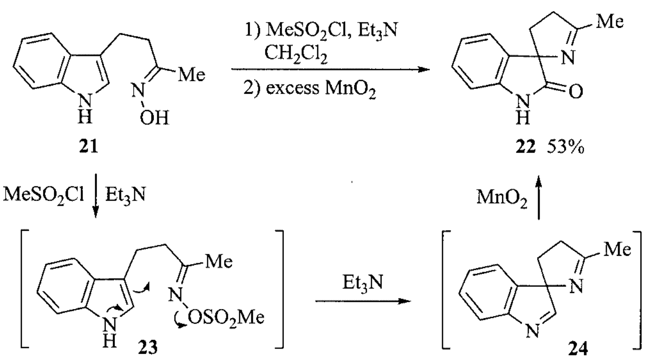
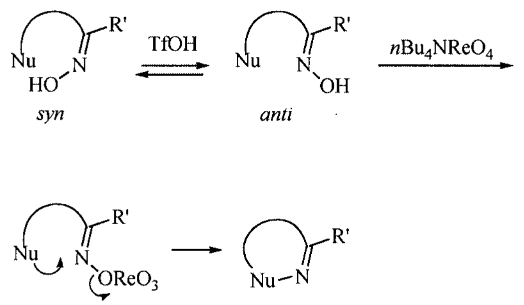


(4)

Spiro[indoline-3,2′-pyrrolidine] **22** was also synthesized by the substitution reaction of oximes [Equation (4)]. When *anti*-β-3-indolyl ketone oxime **21** was treated withmethanesulfonyl chloride and triethylamine, *O*-sulfonylation and the successive nucleophilic attack of the 3-position of the indole ring occurred to give spiro imine **24**, which was oxidized to spiro[pyrrolidine-2.3′-oxindole] **22** with excess MnO_2 in a one-pot procedure.[12]

In these S_N2-type reactions, only *anti* oximes could be converted to the cyclization products. Only the exception is the $n\mathrm{Bu_4ReO_4}$–TfOH promoted cyclization of phenethyl ketone oximes, because the *syn-anti* isomerization of oximes takes place with the action of a protonic acid such as TfOH (Scheme 5).

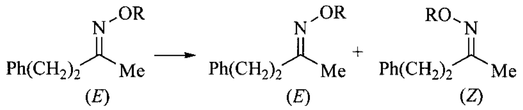


Scheme 5.

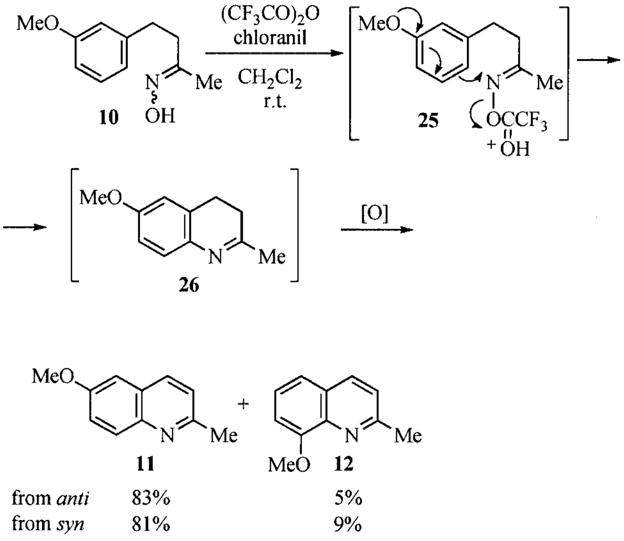
Syn and *anti* oximes readily isomerize with acid, whereas the isomerization of *O*-substituted oximes hardly occurs under acidic conditions. This was a big hurdle for the application of the S_N2-type reaction to prepare cyclic imines, because it is quite hard to prepare oxime derivatives in a stereoselective manner. As it was desirable to employ both stereoisomers for the S_N2-type cyclization, the *syn-anti* isomerization (*E-Z* isomerization) of *O*-substituted oximes was studied (Table 1).[13] (*E*)-4-Phenylbutan-2-one oxime isomerized with the action of TfOH, while the *O*-methyloxime did not under the same conditions (runs 1 and 2). *O*-Methyloxime was found to isomerize by the combined use of TfOH and a nucleophile such as methanol (run 3), probably due to the protonation of the oxime nitrogen and the successive addition-elimination of methanol to the imino group. In addition, *O*-acyloximes such as *O*-acetyloxime were isomerized by the action of a carboxylic acid, but slowly (run 4). *O*-Acyloximes having a more labile *O*-acyl group, such as a trifluoroacetyl group, isomerized with trifluoroacetic acid at room temperature to rapidly attain the equilibrium of *E* and *Z* isomers (run 5). The isomerization of this labile *O*-acyloxime proceeds not only by the above-mentioned addition-elimination mechanism, but also by an alternative mechanism, based on the following observation. The treatment of acetone *O*-(chlorodifluoroacetyl)oxime with trifluoroacetic acid resulted in the generation of a mixture of the *O*-(trifluoroacetyl)- and *O*-(chlorodifluoroacetyl)oximes. The scrambling of acyl groups indicated that the isomerization also occurred by the S_N2 substitution at the oxime nitrogen with acids and/or the acyl exchange through the formation of a mixed anhydride and the free oxime.

Based on these findings on the isomerization, the cyclization of each stereoisomer of β-aryl ketone oximes was examined under the isomerization conditions. The *anti* isomer of 4-(2-methoxyphenyl)butan-2-one oxime (*anti*-**10**) was treated with 3 equivalents of trifluoroacetic anhydride in the presence of chloranil (oxidizing reagent of the preliminary cyclization product, dihydroquinoline **26**) at room temperature [Equation (5)]. The cyclization proceeded as expected to give 6-methoxy- and 8-methoxy-2-methylquinolines **11** and **12**, which corresponded to *para* and *ortho* cyclization products, in 83% and 5% yields, respectively. From *syn*-**10**, quinolines **11** and **12** were also formed in 81% and 9% yield, respectively. Thus β-aryl oximes could be cyclized by this simple procedure, irrespective of the stereochemistry of the oximes.

Table 1. Isomerization of *O*-substituted oximes.

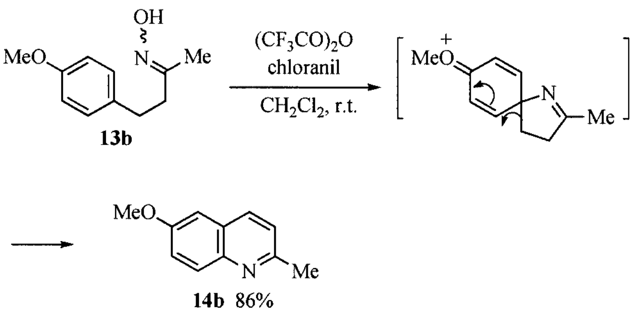


Run	OR	Conditions (equiv.)	(*E*)/(*Z*)
1	OH	CF_3SO_3H (2.0), CH_2Cl_2, r.t., < 20 min	2:1
2	OMe	CF_3SO_3H (2.0), CH_2Cl_2, r.t., 12 h	>99:<1
3	OMe	CF_3SO_3H (2.0), CD_3OD (2.0), CH_2Cl_2, r.t., 12 h	2:1
4	OAc	$PhCO_2H$, toluene, 80 °C, 6 h	3:1
5	$OCOCF_3$	CF_3CO_2H, $CDCl_3$, r.t., 28 h	3:1



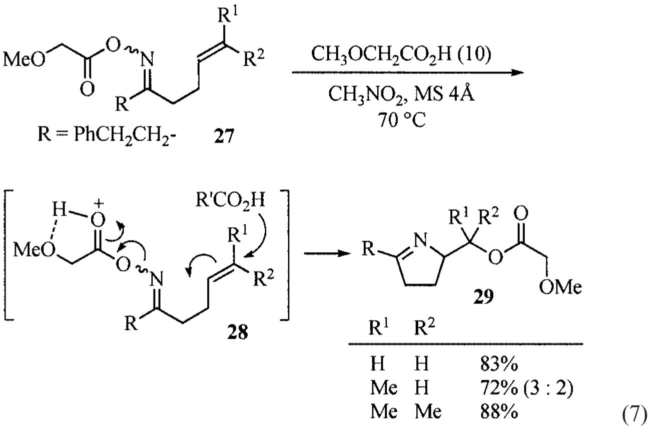
(5)

This cyclization method found wide applicability, and a variety of *para*-substituted or non-substituted phenethyl ketone oximes were converted to quinolines [Equation (6)]. In the rhenium reagent-catalyzed cyclization, as mentioned before, β-*para*-methoxyphenyl ketone oximes were converted to aza-spirotrienones (Scheme 3), while quinolines were obtained predominantly under trifluoroacetic anhydride conditions



(6)

Alkenyl groups as well as aryl groups acted as intramolecular nucleophiles for the cyclization, and γ,δ-unsaturated *O*-(methoxyacetyl)oximes **27** were transformed to 2*H*-dihydropyrroles with the action of methoxyacetic acid [Equation (7)]. Although the olefinic moieties at the γ,δ-position were restricted to being electron rich, various 2*H*-dihydropyrroles were synthesized in good yield.

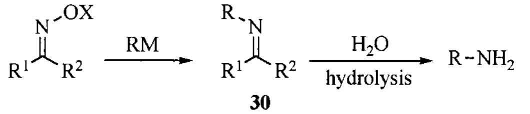


R¹	R²	
H	H	83%
Me	H	72% (3 : 2)
Me	Me	88%

(7)

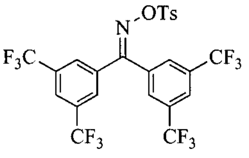
Electrophilic Amination of Grignard Reagents

Primary amines are an important class of amino sources to synthesize various nitrogen-containing biologically active substances and fine chemicals. Generally, primary amines are prepared by alkylation of nucleophilic amination reagents such as potassium phthalimidate (nucleophilic amination)[14] or the reduction of nitrogen-containing compounds having nitro or cyano groups.[15] Recently, transition metal-catalyzed aminations have been developed,[16] some of which have been applied to the synthesis of primary amines.[17] The amination of organometallic reagents with electrophilic nitrogen species such as hydroxylamine derivatives (electrophilic amination) has been studied,[18] however, this method has rarely been employed in organic synthesis as compared with the former methods. Since the intramolecular nucleophilic substitution at sp^2 nitrogen of oximes occurred easily in an S$_N$2 manner, we tried to prepare primary amines by the intermolecular substitution at oxime nitrogen with organometallic reagents and the successive hydrolysis of the resulting *N*-alkylimines **30** (Scheme 6).



Scheme 6.

Some examples of electrophilic aminations with oxime derivatives have been reported for the synthesis of primary amines, but these remain impractical due to the use of excess amounts of organometallic reagents, over-alkylation, and the low product yield.[19] We examined the amination of Grignard reagents with oxime derivatives such as bis[3,5-bis(trifluoromethyl)phenyl] ketone *O*-tosyloxime (**31**)[20] or 1,3-dimethyl-2-imidazolidinone *O*-tosyloxime (**32**).[21] Primary amines were prepared in high yield with wide generality, but modifications of these oximes were required because the bulky substituents such as 3,5-bis(trifluoromethyl)phenyl groups were not appropriate for atom economy, and the hydrolysis of the resulting imines derived from **32** required harsh basic conditions (CsOH, ethylene glycol, 150 °C).



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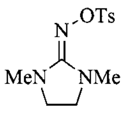

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4,4,5,5-Tetramethyl-1,3-dioxolan-2-one *O*-(phenylsulfonyl)oxime (**33**) was found to be suitable for the amination of Grignard reagents (Table 2).[22] Various Grignard reagents reacted with oxime **33** in non-polar solvents to give the corresponding imines **34**, which were hydrolyzed under acidic conditions to afford primary amines. Aryl Grignard reagents, regardless of the steric congestion and the electronic effect of the substituents on the aryl group, were smoothly aminated with **33**, and anilines were obtained after the hydrolysis of the resulting *N*-aryl imines. Primary, secondary, and tertiary alkylamines were prepared in high yield from the corresponding alkyl Grignard reagents, and even alkenyl Grignard reagents reacted with **33** to give 2-aza-1,3-dienes.

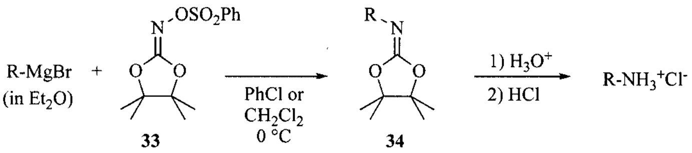
Radical Cyclization

It was supposed that the combination of nucleophiles and leaving groups would be important to promote the S$_N$2-type substitution at the oxime nitrogen, and the cyclization of 2-(3-hydroxyphenyl)ethyl ketone oximes was examined by introducing various leaving groups on the oxime nitrogen. When a mixture of (*E*) and (*Z*)-*O*-(methylsulfonyl) oximes **35** was treated with excess NaH, 6- and 8-quinolinols (**36** and **37**) were obtained in low yield [Equation (8)].[23]

In contrast, the similar reaction of *O*-(2,4-dinitrophenyl) oxime **38** yielded 8-quinolinol **37** and its tetrahydro derivative **40** in high yield without forming the 6-quinolinol [Equation (9)].[24] More interestingly, either the *E*- or the *Z*-isomer of **38** smoothly cyclized to give 8-quinolinols **37** and **40**.

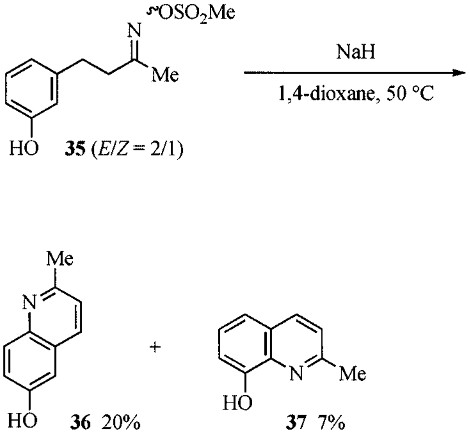
The smooth cyclization of both (*E*)- and (*Z*)-*O*-(2,4-dinitrophenyl) derivatives was not explained simply by an S$_N$2-type reaction. There were two possibilities: either *E*,*Z*-isomerization occurred under the reaction conditions or another reaction pathway was included. To check the isomerization, the *Z*-isomer of β-phenyl *O*-(2,4-dinitrophenyl)oxime (**41**), which had no hydroxy group on the phenyl group, was treated with NaH and *m*-cresol in [D$_8$]THF [Equation (10)]. The isomerisation of *Z*-**41** hardly occurred, while azine **43** and ketone **44** were obtained in 27% and 24% yield, respectively, after quenching with water. Azine **43** might be formed by the dimerization of iminyl radical species **42** (or

Table 2. Amination of Grignard reagents with oxime **33**.



R	% Yield	R	% Yield
Ph	93	$PhCH_2CH_2$	90
p-CF_3-C_6H_4	94	$PhCH_2CH(CH_3)$	89
2,4-$(MeO)_2$-C_6H_3	91	1-Adamantyl	89
2,6-Me_2-C_6H_3	90	CH_2=$CH(CH_3)$– [a]	93

[a] Isolated as imine **34**.



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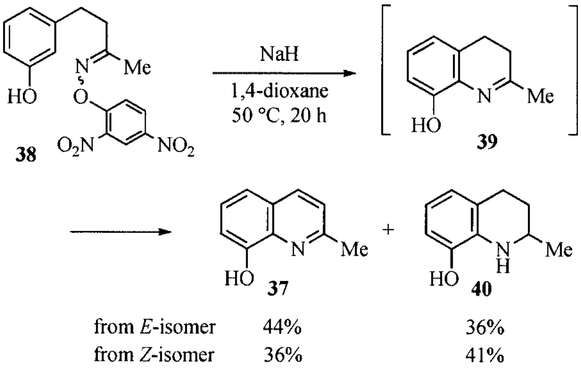

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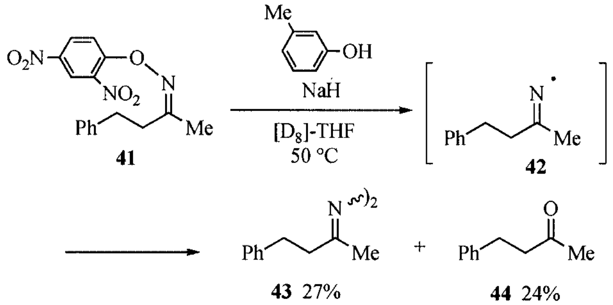


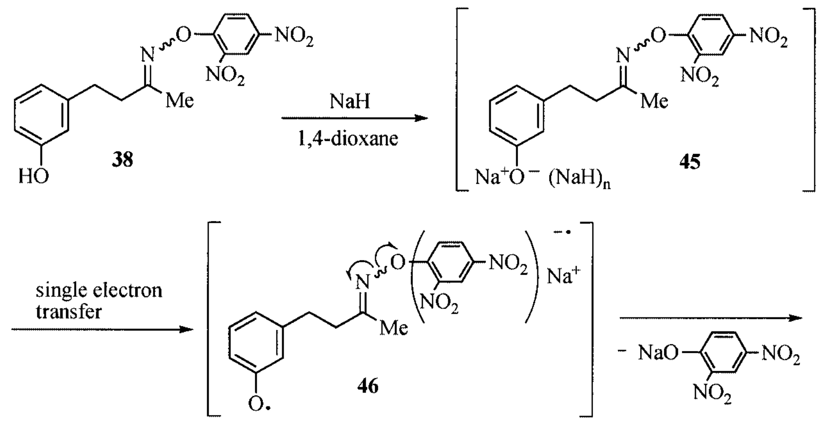
(10)

the equivalent), and the ketone was resulted by the hydrolysis of the imine generated by the hydrogen abstraction of **42**.

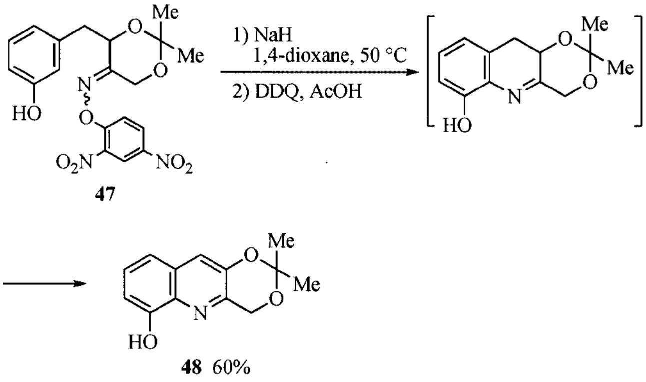
After several further investigations, it was found that the complex of phenoxide and excess NaH worked as a good electron donor, and quinolines **37** and **40** were formed by a radical process induced by electron transfer, as shown in Scheme 7. Intramolecular single electron transfer occurs in **45** from the phenoxide–excess NaH complex to the dinitrophenyl group to generate the anion radical species **46**, from which radical coupling between the phenoxyl radical and the oxime nitrogen proceeds with the elimination of 2,4-dinitrophenoxide.

This cyclization reaction has high utility because both stereoisomers of *O*-(2,4-dinitrophenyl)oximes can be employed in the synthesis of quinolinols, however, two products (quinolinols and tetrahydro derivatives) are always produced as disproportionated products of the initially-formed dihydroquinolinol **39**. It was desirable to obtain each product selectively. 8-Quinolinols could be prepared exclusively from 2-(3-hydroxyphenyl)ethyl ketone *O*-(2,4-dinitrophenyl)oximes by the radical cyclization and the successive one-pot oxidation with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) and acetic acid [Equation (11)].[23] When the cyclization was carried out with NaH in the presence of a reducing reagent, $NaBH_3CN$, tetrahydro-8-qunolinols were obtained instead of quinolinols [Equation (12)].[25] Both methods exhibited wide generality and various 8-quinolinols and tetrahydro-8-quinolinols were synthesized selectively from β-(3-hydroxyphenyl) oximes.

Thus *m*-hydroxyphenethyl ketone oximes are transformed to 8-quinolinol derivatives by the cyclization of iminyl radical equivalents generated by intramolecular electron transfer. In aza-heterocycle synthesis, oxime derivatives have been used as the sources of iminyl radical reactive intermediates.[26] For example, Forrestor et al. reported the synthesis of quinolines by the cyclization of the iminyl radical formed by the oxidation of an *O*-(hydroxycarbonylmethyl)oxime [Equation (13)].[27] Zard et al. have extensively studied the generation of iminyl radical species from



Scheme 7.



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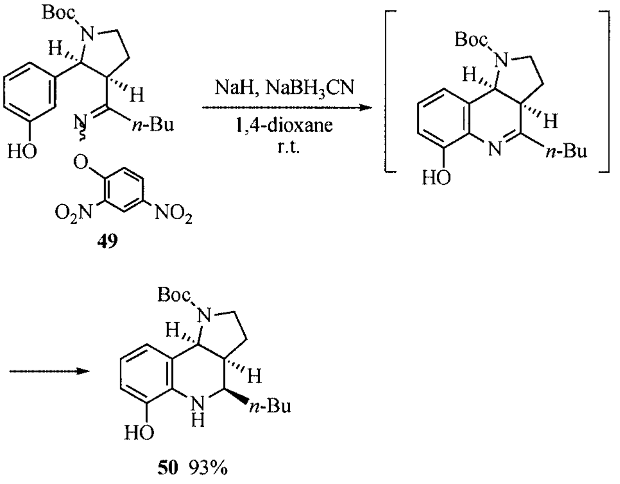
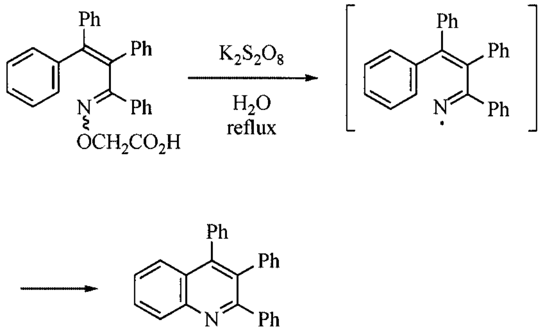


(12)

oximes and their addition reactions to internal alkenes.[28,29] Various methods have been developed for the generation of iminyl radical species, such as the action of $n\mathrm{Bu_3SnH}$/AIBN on *O*-substituted oximes [Equation (14)], the reduction of *O*-acetyloxime with nickel powder, and so on. Weinreb recently devised an efficient cyclization method of *O*-(2,6-dimethylphenylsulfinyl)oximes by applying the Hudson reaction [Equation (15)].[30]



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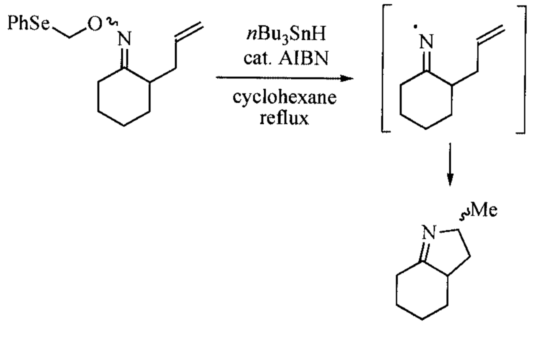
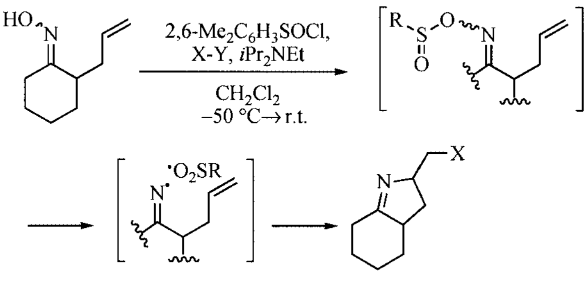
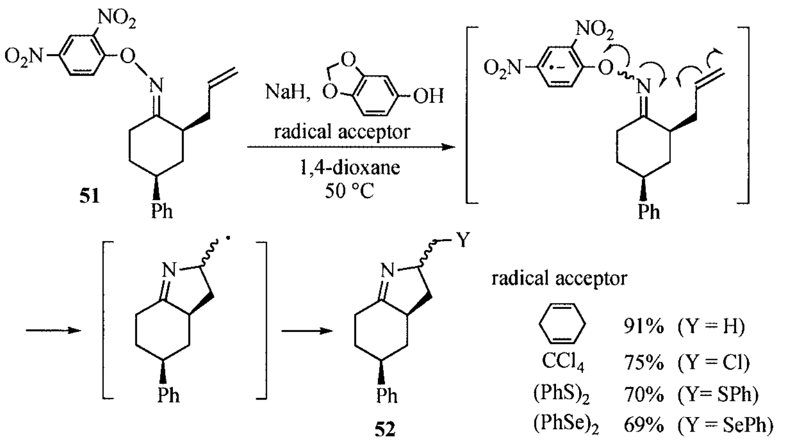


(14)



X-Y = $(\mathrm{PhSe})_2$, $(\mathrm{PhS})_2$, TEMPO, 1,4-cyclohexadiene (15)



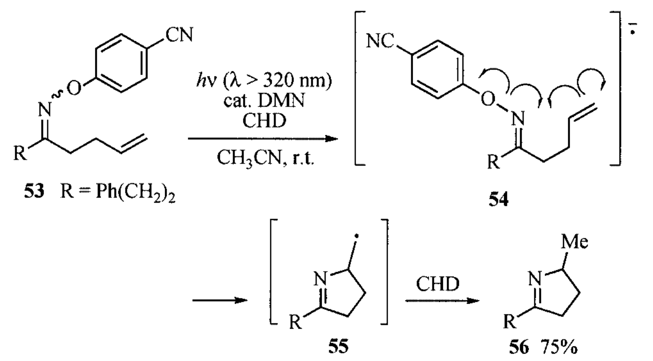
Scheme 8.

The quinoline formation from 2,4-dinitrophenyl-oximes prompted us to study the radical cyclization of γ,δ-unsaturated *O*-(2,4-dinitrophenyl)oximes. In this case, the addition of an electron donor is required, and the combination of 3,4-methylenedioxyphenol (sesamol) and excess amounts of NaH was found to work efficiently for the cyclization. The treatment of *cis*-2-allyl-4-phenylcyclohexanone (*E*)-*O*-(2,4-dinitrophenyl)oxime (**51**) with NaH, sesamol, and 1,4-cyclohexadiene (CHD) in 1,4-dioxane at 50 °C afforded cyclic imine **52** in 91% yield (Scheme 8).[31] Other radical trapping reagents such as CCl_4, $(PhS)_2$, and $(PhSe)_2$ were also utilized as radical terminators instead of 1,4-cyclohexadiene.

Although it has become apparent that one electron reduction of *O*-(2,4-dinitrophenyl)oximes induces the radical cyclization to afford aza-heterocycles, the reaction has to be performed under strongly basic conditions, and 2,4-dinitrophenyl group is not a good leaving group in the sense of atom economy. Accordingly, we next tried to modify this radical reaction to be a catalytic process.

Photolysis ($\lambda > 320$ nm) of a mixture of γ,δ-unsaturated *O*-(*p*-cyanophenyl)oxime **53** and 1,5-dimethoxynaphthalene (DMN) in acetonitrile yielded 3,4-dihydro-2*H*-pyrrole **56** (Scheme 9).[32] The reaction is initiated by one-electron transfer from the exited DMN to **53**, and the resulting anion radical **54** cyclizes to generate alkyl radical intermediate **55** with the elimination of *p*-cyanophenoxide. Then alkyl radical **55** is trapped with 1,4-cyclohexadiene to yield cyclic imine **56**. To make the electron transfer efficient, the *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 *p*-cyanophenyl group with a small substituent to facilitate the availability of the starting materials.

Of course, γ,δ-unsaturated *O*-acetyloxime **57a** was not cyclized efficiently by photo-induced electron transfer with DMN (the yield of **58a** and **59a** was 4%) because the *O*-acetyloxime did not act as a good electron acceptor. The addition of acetic acid, however, accelerated the photochemical electron transfer reaction, in which the protonated *O*-acetyloxime generated in equilibrium worked as a good electron acceptor. That is, in the presence of 10 equivalents of acetic acid, γ,δ-unsaturated ketone *O*-acetyloxime **57a** cyclized to 4-acetoxymethy-3,4-dihydropyrroles **58a** and **59a** in acetonitrile under photo irradiation ($\lambda > 300$ nm) in the presence of 1,5-dimethoxynaphthalene (DMN) as a catalytic sensitizer (Scheme 10).[33] The addition of a small amount of 1,4-cyclohexadiene (20 mol-%) made the reaction cleaner, and 1,4-cyclohexadiene presumably acted as a scavenger of some radical species such as those generated from the solvent.

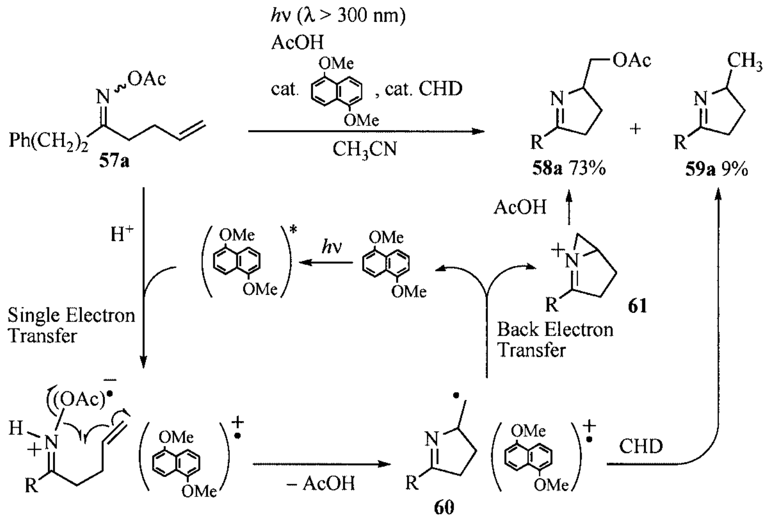


DMN = 1,5-dimethoxynaphthalene, CHD = 1,4-cyclohexadiene

Scheme 9.

This cyclization via photosensitized electron transfer may proceed as follows. Single electron transfer (SET) from excited DMN to protonated oxime **57a** occurs and cyclization with the cleavage of the N–O bond gives alkyl radical species **60**. Back electron transfer (BET) from **60** to the cation radical of DMN regenerates the sensitizer, DMN, and a cationic species like **61** is immediately trapped with AcOH to give acetoxymethyl 2*H*-dihydrpyrrole **58a**. Methylated dihydropyrrole **59a** is formed from alkyl radical species **60** by abstracting hydrogen from 1,4-cyclohexadiene (CHD).

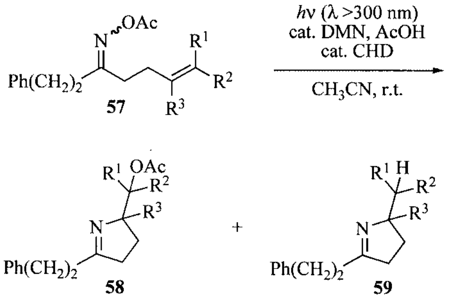
Various γ,δ-unsaturated *O*-acetyloximes of alkyl ketones were converted to dihydropyrroles as shown in Table 3. Although cyclization of **57** having a terminal vinyl group gave acetoxymethyl cyclic imine **58** and a small amount of hydrogenated product **59**(run 1), oximes having an internal alkenyl moiety gave acetoxymethyl imines **58** exclusively (runs



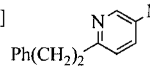
Scheme 10.

2–4). From γ-substituted γ,δ-unsaturated oxime **57**, pyridine **62** was formed through 6-*endo* cyclization in 15% with a 58% total yield of five-membered cyclic imines (run 5).

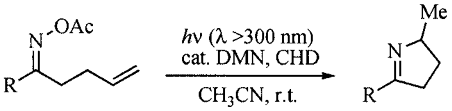
Table 3. Photochemical cyclization of *O*-acetyloximes.



Run	R^1	R^2	R^3	% 58	% 59
1	H	H	H	73	9
2	H	Me	H	82	0
3	H	Ph	H	76	0
4	Me	Me	H	80	0
5[a]	H	H	Me	47	11

[a]  **62** was obtained in 15% yield.

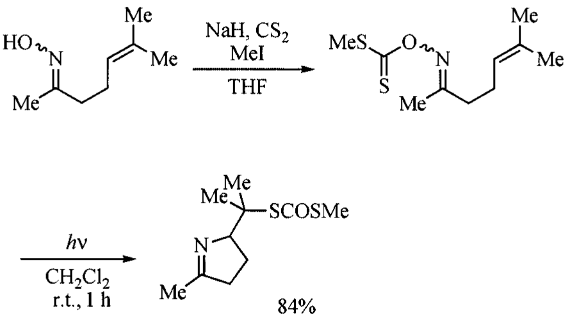
Thus the cyclization of alkyl ketone *O*-acetyloximes **57** proceeded by photosensitized electron transfer in the presence of acetic acid, while acetic acid did not show any effect in the cyclization of aryl and α,β-unsaturated ketone oximes. The cyclization of these conjugated *O*-acetyloximes finished within a shorter time as compared to that of nonconjugated oximes, and 2-methyldihydropyrroles were obtained instead of 2-acetoxymethyl derivatives [Equation (16)]. Because the cyclization proceeded quite slowly in the absence of DMN, the reaction presumably proceeds via energy transfer through the exciplex formation between DMN* and the oximes.



R = Ph	0.5 h	77%
R = $Ph(CH_2)_3O_2C$	2 h	56%
R = (*E*)-Ph-CH=CH$_2$	5 h	63%

(16)

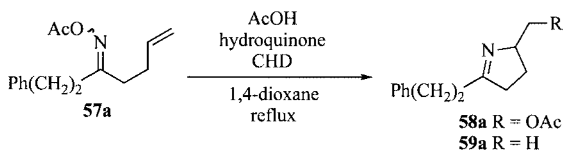
Concerning the photochemical radical reaction of oximes, Zard et al. reported an efficient radical chain cyclization of *O*-(methylthiothiocarbonyl)oxime initiated by homolytic cleavage of the N–O bond by light irradiation [Equation (17)].[29c]



(17)

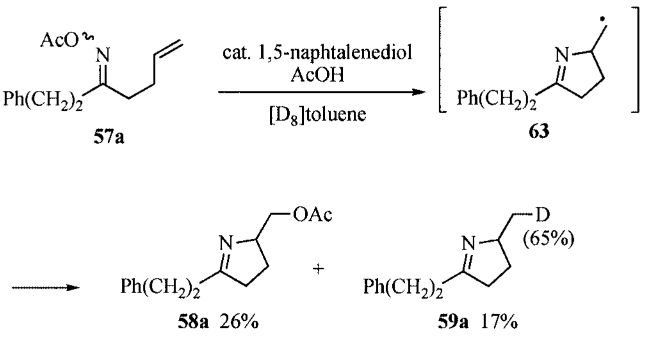
In addition to the photochemical one-electron reduction, exploration of catalytic radical cyclizations of γ,δ-unsaturated *O*-acetyloximes was attempted by employing electron donor catalysts. In the first example, dihydroquinone (or 1,5-naphthalenediol) was employed as a catalyst. When a solution of γ,δ-unsaturated *O*-acetyloxime **57a**, acetic acid, 1,4-cyclohexadiene, and a catalytic amount of hydroquinone in 1,4-dioxane was heated, dihydropyrroles **58a** and **59a** were obtained in 86% total yield (Table 4).[34]

Table 4. Hydroquinone-catalyzed cyclization of *O*-acetyloxime **57a**.



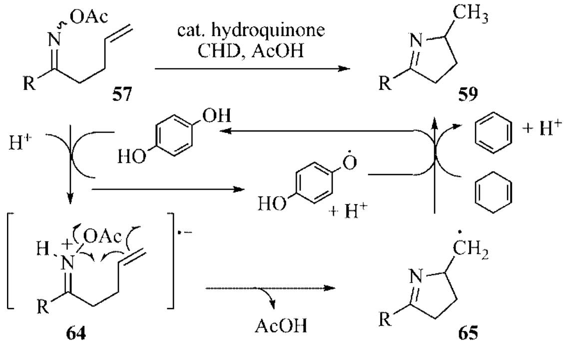
Hydroquinone	CHD	Time/h	% **58a**	% **59a**
none	none	24	19	20
5 mol-%	none	6	22	44
5 mol-%	10 equiv.	6	32	53
none	10 equiv.	24	12	29

The formation of radical intermediate **63** was confirmed by the following trapping experiment. The reaction in [D$_8$]toluene without 1,4-cyclohexadiene afforded the cyclic imine **59a** in 17% yield with 65% deuterium content in the methyl group, along with 26% yield of **58a** [Equation (18)].



(18)

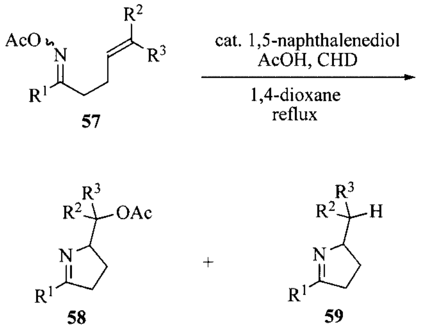
As shown in Scheme 11, one-electron transfer occurs from hydroquinone to the protonated *O*-acetyloxime **57**, and the resulting protonated anion radical **64** cyclizes to generate alkyl radical **65**, which abstracts a hydrogen atom from 1,4-cyclohexadiene. The catalyst, hydroquinone, is regenerated from phenoxyl radical by hydrogen-atom abstraction from 1,4-cyclohexadiene.



Scheme 11.

Reaction of *O*-acetyloxime **57**, having an electron-rich olefinic moiety, yielded acetoxymethyl derivative **58** as a major product by S$_N$2-type cyclization as mentioned before (Table 5, runs 2 and 3). In contrast, only radical cyclization products **59** were obtained from oximes **57** that had electron-deficient olefinic moieties (runs 4 and 5). *O*-Acyloximes of phenyl ketones and α-keto esters also cyclized to give only methylated dihydropyrroles **59** (runs 6 and 7).

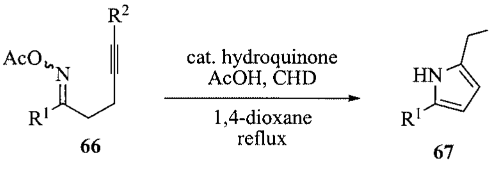
Table 5. Cyclization of various *O*-acetyloximes.



Run	R^1	R^2	R^3	*syn*/*anti*	Time	% **58**	% **59**
1	Ph(CH$_2$)$_2$	H	H	1:1	6 h	34	52
2	Ph(CH$_2$)$_2$	Me	H	1:1	6 h	67	16
3	Ph(CH$_2$)$_2$	Me	Me	1:1	6 h	72	5
4	Ph(CH$_2$)$_2$	CN	H	1:1	12 h	0	69
5	Ph(CH$_2$)$_2$	CO$_2$Et	H	1:2	12 h	0	72
6	Ph	H	H	>99:<1	8 h	0	75
7[a]	Ph(CH$_2$)$_2$O$_2$C	H	H	>99:<1	6 h	0	67

[a] *O*-Pivaloyloxime was used instead of *O*-acetyloxime.

This method could be applied to the preparation of pyrroles from γ,δ-unsaturated *O*-acetyloximes having an alkynyl moiety as shown in Equation (19).[34b] Both alkyl and aryl ketoximes **66** having a terminal alkynyl group were converted to 2,5-disubstituted pyrroles **67** in good yield. No significant influence was observed by the introduction of terminal substituent on the alkynyl group.

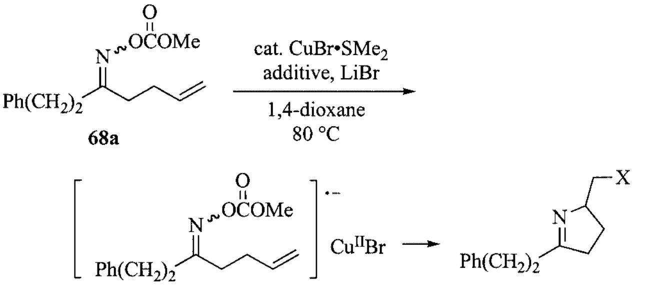


R^1	R^2	
Ph(CH$_2$)$_2$	H	67%
Ph	H	67%
Ph	Me	72%
Ph	CO$_2$Et	83%

(19)

It was expected that one-electron reduction of oxime derivatives would proceed by treatment with low valent transition metal compounds. As mentioned previously, such an example was reported by Zard. That is, the treatment of γ,δ-unsaturated *O*-acetyloximes with nickel powder and acetic acid in 2-propanol leads to the cyclization to dihydropyrroles.[28c] The reaction, however, requires large excess amounts of nickel powder, and it is desirable to conduct such a transformation in a catalytic manner.

Copper(I) was found to work as a redox catalyst.[35] When a *syn*/*anti* (1:1) mixture[2] of *O*-(methoxycarbonyl)oxime of γ,δ-unsaturated ketone **68a** and 5 mol-% of $CuBr{\cdot}SMe_2$ in 1,4-dioxane was heated to 80 °C, cyclic imine **59a** was obtained in 39% yield [Equation (20)]. 4-Bromomethyl-3,4-dihydropyrrole **70a** was obtained and the product yield was much improved (to 86%) by the addition of LiBr. *O*-(pentafluorobenzoyl)oxime was also was cyclized in high yield, whereas the corresponding *O*-(2,4-dinitrophenyl)- and *O*-acetyloximes were not appropriate for the $CuBr{\cdot}SMe_2$–LiBr-catalyzed cyclization. The reaction probably proceeds by electron transfer from the copper(I) salt to the oxime **68a**, generating anion radical **69**, which in turn cyclizes to give **70a** with the elimination of Cu^I methyl carbonate.

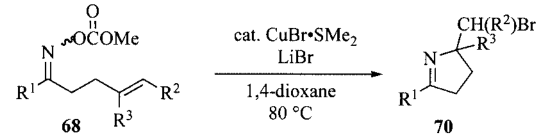


additive	
none	39% (**59a**, X = H)
LiBr	86% (**70a**, X = Br)

(20)

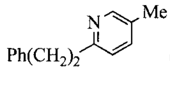
As listed in Table 6, the catalytic process with $CuBr{\cdot}SMe_2$–LiBr could be applied to the cyclization of various γ,δ-unsaturated ketone *O*-(methoxycarbonyl)oximes. Cyclization of oximes having an γ,δ-disubstituted alkenyl moiety gave cyclic imines in high yield (runs 1 and 2). From the γ-methyl-substituted oxime, a 5,5-disubstituted dihydropyrrole was obtained in 53% yield along with 16% yield of disubstituted pyridine **62** (run 3). Phenyl ketone and α-keto ester oximes were smoothly transformed into 2-phenyl and 2-ethoxycarbonyl dihydropyrroles, respectively (runs 4 and 5).

Table 6. $CuBr{\cdot}SMe_2$-catalyzed cyclization of *O*-methoxycarbonyloximes.



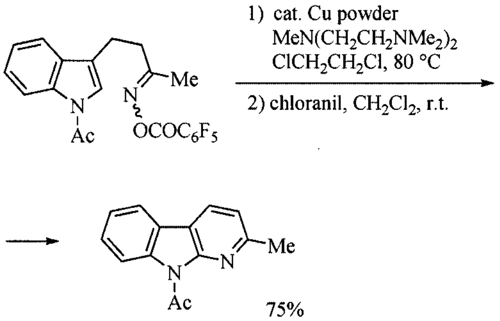
Run	R^1	R^2	R^3	% Yield
1	$Ph(CH_2)_2$	Me	H	85
2	$Ph(CH_2)_2$	Ph	H	74
3[a]	$Ph(CH_2)_2$	H	Me	53
4	Ph	H	H	83
5	CO_2Et	H	H	53

[a]



62 was obtained in 16% yield.

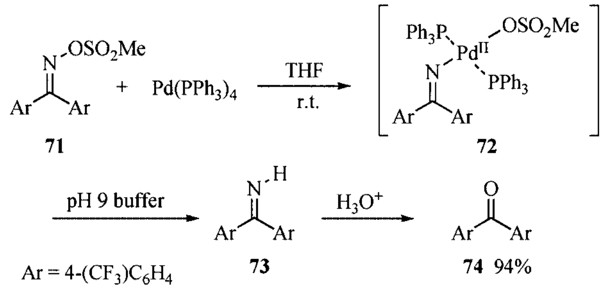
Furthermore, α-carbolines were prepared by the radical cyclization of β-3-indolyl ketone *O*-(pentafluorobenzoyl)oximes by treatment with a catalytic amount of copper powder in dichloroethane and successive oxidation with chloranil [Equation (21)].[36] In this radical cyclization, copper powder gradually reacted with 1,2-dichloroethane to generate the copper(I) salt, which acts as an active redox catalyst.



(21)

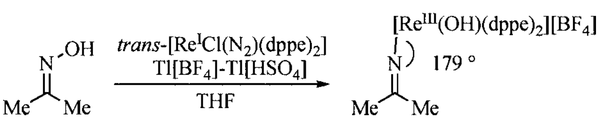
Amino-Heck Reaction[37]

As lower-valent palladium compounds are good electron donors, oxime derivatives were expected to react with Pd^0 complexes, giving oxidative addition compounds, alkylideneaminometal species. In fact, an equimolar amount of 4,4′-bis(trifluoromethyl)benzophenone *O*-(methylsulfonyl) oxime (**71**) and $Pd(PPh_3)_4$ reacted in tetrahydrofuran (THF) at room temperature, and, after quenching with a pH 9 buffer, 4,4′-bis(trifluoromethylphenyl)methylideneamine (**73**) was obtained as a crude product.[38] Compound **73** was hydrolyzed to benzophenone **74** in 94% overall yield by acid treatment (Scheme 12). This result indicates that diarylmethylideneaminopalladium(II) intermediate **72** was formed by the oxidative addition of **71** to $Pd(PPh_3)_4$ and then hydrolyzed to imine **73**.



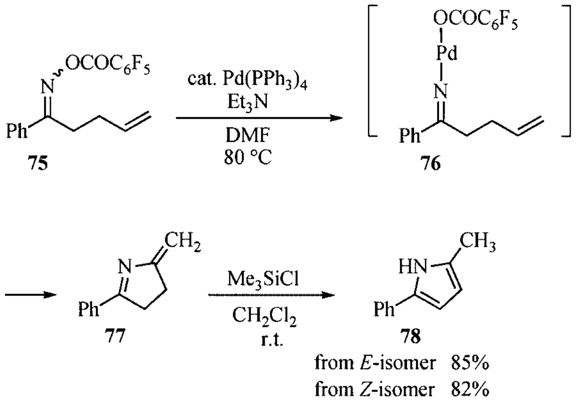
Scheme 12.

Although we could not isolate alkylideneaminopalladium(II) species **72**, Pombeiro et al.[39] and Tillact et al.[40] recently reported the isolation of oxidative addition products of oximes to low-valent rhenium and titanium complexes. The X-ray analysis of the complexes revealed that the bond angle of carbon–nitrogen–metal is, interestingly, almost linear [Equation (22)].



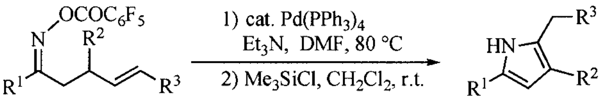
(22)

To utilize this aminopalladium species for organic synthesis, the intramolecular Mizoroki–Heck type reaction (amino-Heck reaction) was investigated (Scheme 13). When γ,δ-unasaturated ketone (*E*)-*O*-(pentafluorobenzoyl)oxime **75** was treated with Et_3N and a catalytic amount of $Pd(PPh_3)_4$ in DMF, 2*H*-3,4-dihydropyrrole **77** was initially formed and then isomerized to pyrrole **78** by treatment with Me_3SiCl in CH_2Cl_2. This amino-Heck reaction was not affected by the geometry of the oximes, and both *E*-oxime **75** and the Z-isomer were smoothly converted to pyrrole **78**, probably due to the linear structure of the alkylideneaminopalladium intermediate **76**. The similar reaction of the *O*-sulfonyloxime also gave the product **78** in 60% yield but with formation of the Beckmann rearrangement product.



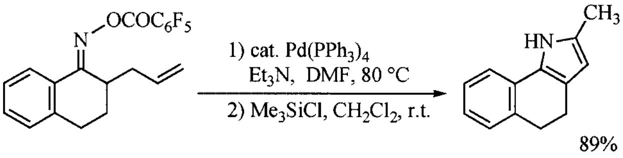
Scheme 13.

Various γ,δ-unsaturated ketone oximes having terminal and disubstituted vinyl groups cyclized to pyrroles smoothly by this amino-Heck reaction [Equations (23) and (24)].



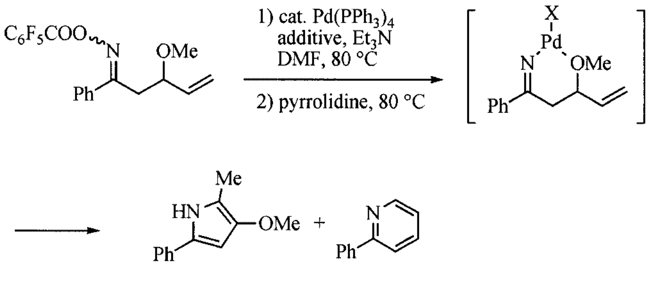
$R^1 = Ph, R^2 = Me, R^3 = H$ 80%
$R^1 = CO_2Et, R^2 = H, R^3 = CO_2Et$ 45%

(23)



(24)

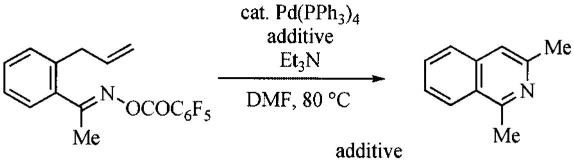
Thus, the 5-*exo* mode cyclization proceeded generally, while the 6-*endo* mode cyclization product was obtained in the reaction of the γ,δ-unsaturated ketone *O*-(pentafluorobenzoyl)oxime having a methoxy group at the β-position (Scheme 14).[41] Particularly, in the presence of nBu$_4$NCl, the pyridine was obtained as a major product. The reaction pathway was not clear, but the cyclization was certainly initiated by the oxidative addition of the oximes to $Pd(PPh_3)_4$.



additive		
none	69%	7%
n-Bu$_4$NCl	11%	58%

Scheme 14.

Isoquinolines were prepared by the 6-*exo* cyclization of *O*-allyl acetophenone oxime derivatives (Scheme 15).[41] In this reaction, addition of nBu$_4$NCl was also effective to improve the yield of isoquinolines.



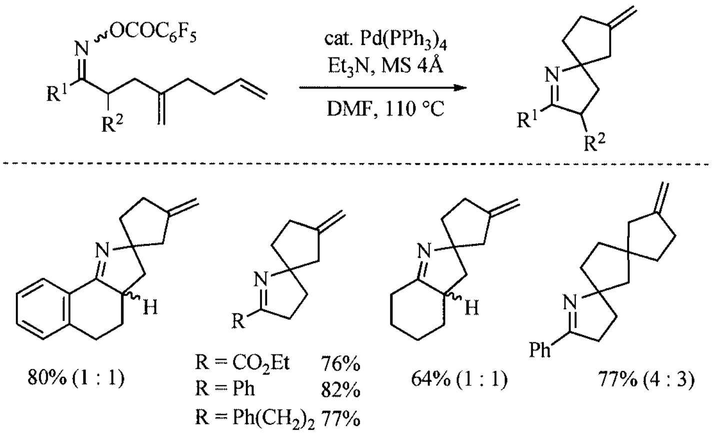
additive	
none	48%
*n*Bu$_4$NCl	77%

Scheme 15.

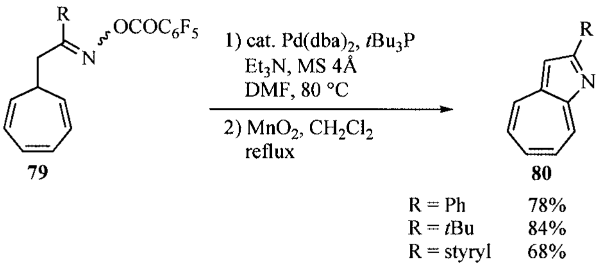
Various methods have been developed towards the construction of the 1-azaspiro[4.4]nonane skeleton.[42] The amino-Heck reaction provided a metal-catalyzed method to prepare spiro bicyclic and tricyclic imines from dienyl and trienyl ketone oximes through a domino cyclization pathway (Scheme 16).[43]

The amino-Heck type reaction was modified to realize a straightforward method for the synthesis of aza-azulenes. 1-Aza-azulenes were obtained by the treatment of cycloheptatrienylmethyl ketone *O*-(pentafluorobenzoyl)oximes **79** with $Pd(dba)_2/P(tBu)_3$ and Et_3N and the successive oxidation of the crude mixture with MnO_2 [Equation (25)].[44]

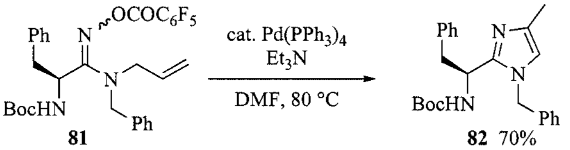
This amino-Heck reaction could be applied to prepare a wide range of heterocycles. For example, 1-benzyl-4-methylimidazoles with a range of substituents at the 2-position were synthesized by the amino-Heck reaction of amidoximes. The palladium-catalyzed amino-Heck cyclization of α-chiral oxime **81** proceeded smoothly without racemization, yielding optically active amino acid mimetics **82**, containing a C-terminal imidazole [Equation (26)].



Scheme 16.



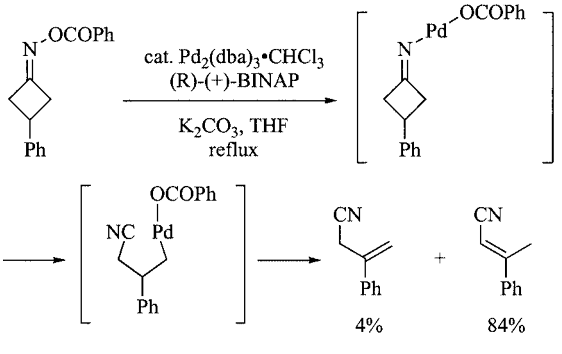
(25)



(26)

Although various aza-heterocycles were prepared from ketoximes by the palladium-catalyzed amino-Heck reaction, some oximes such as aldoxime, alkynyl ketoxime, and α-alkoxy ketoximes could not be cyclized, but transformed to nitriles with C–H and C–C bond cleavage under the palladium-catalyzed conditions.[37]

Uemura et al. reported a similar type of palladium-catalyzed nitrile formation from cyclobutanone oximes [Equation (27)].[45] Ring opening of cyclobutanone *O*-acyloximes occurred from the alkylideneaminopalladium species and successive *β*-hydride elimination yielded nitriles.



(27)

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[1] Recent reviews on oximes: a) E. Abele, E. Lukevics, *Heterocycles* **2000**, *53*, 2285–2336; b) K. Narasaka, M. Yamane, in: *Science of Synthesis* vol. 27: *Carbons with Two Carbon–Heteroatom Bonds: Heteroatom Analogues of Aldehydes and Ketones* (Ed.: A. Padwa), Thieme: Stuttgart, **2004**, chapter 15; c) M. Kitamura, K. Narasaka, *Synth. Org. Chem. Jpn.* **2004**, *62*, 38–48.

[2] a) R. E. Gwley, *Org. React.* **1988**, *35*, 1; b) K. Maruoka, H. Yamamoto, in: *Comprehensive Organic Synthesis: Functional Group Transformations* via *Carbonyl Derivatives* (Eds.: B. M. Trost, I. Fleming), Pergamon: Oxford, **1996**, vol. 6, pp. 763–793; c) L. G. Donaruma, W. Z. Heldt, *Org. React.* **1960**, *11*, 1; d) P. A. S. Smith, in: *Molecular Rearrangements* (Eds.: I. Pert, P. de Mayo), Interscience: New York, **1962**, p. 483.

[3] We previously partially reviewed this topic: a) K. Narasaka, *Pure Appl. Chem.* **2003**, *75*, 19–28; b) K. Narasaka, *Pure. Appl. Chem.* **2002**, *74*, 143–149.

[4] a) K. Narasaka, H. Kusama, Y. Yamashita, H. Sato, *Chem. Lett.* **1993**, 489–492; b) H. Kusama, Y. Yamashita, K. Narasaka, *Bull. Chem. Soc. Jpn.* **1995**, *62*, 373–377.

[5] a) H. Kusama, Y. Yamashita, K. Narasaka, *Chem. Lett.* **1995**, 5–6; b) H. Kusama, K. Uchiyama, Y. Yamashita, K. Narasaka, *Chem. Lett.* **1995**, 715–716; c) H. Kusama, Y. Yamashita, K. Uchiyama, K. Narasaka, *Bull. Chem. Soc. Jpn.* **1997**, *70*, 965–975.

[6] D. Schinzer, Y. Bo, *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 687–688.

[7] a) M. Hamana, H. Noda, J. Uchida, *Yakugaku Zasshi* **1970**, *90*, 991; b) D. H. R. Barton, B. W. Motherwell, S. E. Simon, S. Z. Zard, *J. Chem. Soc., Chem. Commun.* **1984**, 337; c) Y. Ishida, S. Sasatani, K. Maruoka, H. Yamamoto, *Tetrahedron Lett.* **1983**, *24*, 3255–3258.

[8] a) G. M. Rishton, M. A. Schwartz, *Tetrahedron Lett.* **1988**, *29*, 2643–2646; b) M. Kobayashi, K. Uneyama, N. Hamada, S. Kashino, *Tetrahedron Lett.* **1994**, *35*, 5235–5238.

[9] a) Z. Rappoport, *Acc. Chem. Res.* **1992**, *25*, 474–479; b) T. Okuyama, G. Lodder, in: *Advances in Physical Organic Chemistry* (Eds.: T. T. Tidwell, J. P. Richard), Academic Press: New York, **2002**; vol. 37, pp. 1–56.

[10] a) S. Mori, K. Uchiyama, Y. Hayashi, K. Narasaka, E. Nakamura, *Chem. Lett.* **1998**, 111–112; b) K. Uchiyama, M. Yoshida, Y. Hayashi, K. Narasaka, *Chem. Lett.* **1998**, 607–608; c) M. Yoshida, K. Uchiyama, K. Narasaka, *Heterocycles* **2000**, *52*, 681–691.

[11] In this manuscript, *syn*-oxime means the hydroxy, alkoxy or acyloxy group on the oxime nitrogen and a nucleophilic moiety

are in the same side of the oxime C=N bond, and *anti* means they are on the opposite sides.

[12] K. Tanaka, Y. Mori, K. Narasaka, *Chem. Lett.* **2004**, *33*, 26–27.

[13] M. Kitamura, M. Yoshida, T. Kikuchi, K. Narasaka, *Synthesis* **2003**, 2415–2426.

[14] a) S. Gabriel, *Ber. Dtsch. Chem. Ges.* **1887**, *20*, 2224; b) M. S. Gibson, R. W. Bradshaw, *Angew. Chem. Int. Ed. Engl.* **1968**, *7*, 919–930; c) R. A. W. Johnstone, D. W. Payling, C. Thomas, *J. Chem. Soc., C* **1969**, 2223; d) U. Ragnarsson, L. Grehn, *Acc. Chem. Res.* **1991**, *24*, 285–289.

[15] a) H. O. House, *Modern Synthetic Reactions*, 2nd ed., Benjamin: California, **1972**; b) G. W. Kabalka, in: *Comprehensive Organic Synthesis* (Ed.: B. M. Trost), Pergamon: Oxford, **1991**, vol. 8, p. 363; c) R. O. Hutchins, M. K. Hutchins, in: *Comprehensive Organic Synthesis* (Ed.: B. M. Trost), Pergamon: Oxford, **1991**, vol. 8, p. 25; d) O. Mitsunobu, in: *Comprehensive Organic Synthesis* (Ed.: B. M. Trost), Pergamon: Oxford, **1991**, vol. 6, pp. 65–101.

[16] a) J. P. Wolfe, S. Wagaw, J.-F. Marcoux, S. L. Buchwald, *Acc. Chem. Res.* **1998**, *31*, 805–818; b) J. F. Hartwig, *Acc. Chem. Res.* **1998**, *31*, 852–860; c) J. F. Hartwig, *Angew. Chem. Int. Ed.* **1998**, *37*, 2046–2067.

[17] a) J. P. Wolfe, J. J. Åhman, P. Sadighi, R. A. Singer, S. L. Buchwald, *Tetrahedron Lett.* **1997**, *38*, 6367–6370; b) G. Mann, J. F. Hartwig, M. S. Driver, C. Fernández-Rivas, *J. Am. Chem. Soc.* **1998**, *120*, 827–828.

[18] a) A. Casarini, P. Dembech, D. Lazzari, E. Marini, G. Reginato, A. Ricci, G. Seconi, *J. Org. Chem.* **1993**, *58*, 5620–5623; b) C. Greck, J. P. Genêt, *Synlett* **1997**, 741–748; c) E. Erdik, M. Ay, *Chem. Rev.* **1989**, *89*, 1947–1980; d) P. Dembech, G. Seconi, A. Ricci, *Chem. Eur. J.* **2000**, *6*, 1281–1286.

[19] a) R. A. Hagopian, M. J. Therien, J. R. Murdoch, *J. Am. Chem. Soc.* **1984**, *106*, 5753–5754; b) E. Erdik, M. Ay, *Synth. React. Inorg. Met.-org. Chem.* **1989**, *19*, 663–668; c) E.-U. Würthwein, R. Weigmann, *Angew. Chem. Int. Ed. Engl.* **1987**, *26*, 923–924; d) E. Erdik, T. Daskapan, *Synth. Commun.* **1999**, *29*, 3989–3997; e) E. Erdik, T. Daskapan, *J. Chem. Soc., Perkin Trans. 1* **1999**, 3139–3142.

[20] a) H. Tsutsui, Y. Hayashi, K. Narasaka, *Chem. Lett.* **1997**, 317–318; b) H. Tsutsui, T. Ichikawa, K. Narasaka, *Bull. Chem. Soc. Jpn.* **1999**, *72*, 1869–1878.

[21] M. Kitamura, S. Chiba, K. Narasaka, *Bull. Chem. Soc. Jpn.* **2003**, *76*, 1063–1070.

[22] M. Kitamura, T. Suga, S. Chiba, K. Narasaka, *Org. Lett.* **2004**, *6*, 4619–4621.

[23] K. Uchiyama, A. Ono, Y. Hayashi, K. Narasaka, *Bull. Chem. Soc. Jpn.* **1998**, *71*, 2945–2955.

[24] K. Uchiyama, Y. Hayashi, K. Narasaka, *Synlett* **1997**, 445–446.

[25] A. Ono, K. Uchiyama, Y. Hayashi, K. Narasaka, *Chem. Lett.* **1998**, 437–438.

[26] a) A. G. Fallis, I. M. Brinza, *Tetrahedron* **1997**, *53*, 17543–17594; b) T. Mikami, K. Narasaka, in: *Advances in Free Radical Chemistry* (Ed.: S. Z. Zard), JAI: Stamford, **1999**; vol. 2, pp. 45–88; c) L. Stella, in: *Radicals in Organic Synthesis* (Eds.: P. Renaud, M. P. Sibi), Wiley-VCH: Weinheim, **2001**; vol. 2, pp 407–426.

[27] a) A. R. Forrester, M. Gill, J. S. Sadd, R. H. Thomson, *J. Chem. Soc., Perkin Trans. 1* **1979**, 612–615; b) S. Atmaram, A. R. Forrester, M. Gill, R. H. Thomson, *J. Chem. Soc., Perkin Trans. 1* **1981**, 1721–1724.

[28] a) J. Boivin, A.-C. Callier-Dublanchet, B. Quiclet-Sire, A.-M. Schiano, S. Z. Zard, *Tetrahedron* **1995**, *51*, 6517–6528; b) S. Z. Zard, *Synlett* **1996**, 1148–1154; c) J. Boivin, A.-M. Schiano, S. Z. Zard, H. Zhang, *Tetrahedron Lett.* **1999**, *40*, 4531–4534.

[29] a) J. Boivin, E. Fouquet, S. Z. Zard, *Tetrahedron Lett.* **1991**, *32*, 4299–4302; b) M. C. Fong, C. H. Schiesser, *Tetrahedron Lett.* **1993**, *34*, 4347–4348; c) J. Boivin, E. Fouquet, A.-M. Schiano, S. Z. Zard, *Tetrahedron* **1994**, *50*, 1769–1776; d) F. Gagosz, S. Z. Zard, *Synlett* **1999**, 1978–1980.

[30] a) X. Lin, D. Stien, S. M. Weinreb, *Org. Lett.* **1999**, *1*, 637–640; b) X. Lin, G. D. Artman III, D. Stien, S. M. Weinreb, *Tetrahedron* **2001**, *57*, 8779–8791.

[31] a) K. Uchiyama, Y. Hayashi, K. Narasaka, *Chem. Lett.* **1998**, 1261–1262; b) K. Uchiyama, Y. Hayashi, K. Narasaka, *Tetrahedron* **1999**, *55*, 8915–8930.

[32] a) T. Mikami, K. Narasaka, *Chem. Lett.* **2000**, 338–339; b) T. Mikami, K. Narasaka, *C. R. Acad. Sci. Paris, Ser. IIc, Chim.* **2001**, *4*, 477–485.

[33] M. Kitamura, Y. Mori, K. Narasaka, *Tetrahedron Lett.* **2005**, *46*, 2373–2376.

[34] a) M. Yoshida, M. Kitamura, K. Narasaka, *Chem. Lett.* **2002**, 144–145; b) M. Yoshida, M. Kitamura, K. Narasaka, *Bull. Chem. Soc. Jpn.* **2003**, *76*, 2003–2008.

[35] Y. Koganemaru, M. Kitamura, K. Narasaka, *Chem. Lett.* **2002**, 784–785.

[36] K. Tanaka, M. Kitamura, K. Narasaka, *Bull. Chem. Soc. Jpn.* in press.

[37] M. Kitamura, K. Narasaka, *Chem. Rec.* **2002**, *2*, 268–277.

[38] a) H. Tsutsui, K. Narasaka, *Chem. Lett.* **1999**, 45–46; b) H. Tsutsui, M. Kitamura, K. Narasaka, *Bull. Chem. Soc. Jpn.* **2002**, *75*, 1451–1460.

[39] a) C. M. P. Ferreira, M. F. C. Guedes da Silva, V.-Yu. Kukushkin, J. J. R. Fraústo da Silva, A. J. L. Pombeiro, *J. Chem. Soc., Dalton Trans.* **1998**, 325–326; b) V.-Yu. Kukushkin, J. J. R. Pombeiro, *Coord. Chem. Rev.* **1999**, *181*, 147–175.

[40] A. Tillack, P. Arndt, A. Spannenberg, R. Kempe, U. Rosenthal, *Z. Anorg. Allg. Chem.* **1998**, *624*, 737–740.

[41] H. Tsutsui, K. Narasaka, *Chem. Lett.* **2001**, 526–527.

[42] a) M. F. Semmelhack, B. P. Chong, R. D. Stauffer, T. D. Rogerson, A. Chong, L. D. Jones, *J. Am. Chem. Soc.* **1975**, *97*, 2507–2516; b) N. Isano, M. Mori, *J. Org. Chem.* **1995**, *60*, 115–119; c) S. Yasuda, T. Yamada, M. Hanaoka, *Tetrahedron Lett.* **1986**, *27*, 2023–2026; d) C.-K. Sha, J.-J. Young, C.-P. Yeh, S.-C. Chang, S.-L. Wang, *J. Org. Chem.* **1991**, *56*, 2694–2696; e) H. Ishibashi, M. Okano, H. Tamaki, K. Maruyama, T. Yakura, M. Ikeda, *J. Chem. Soc., Chem. Commun.* **1990**, 1436–1437; f) L. F. Tietze, H. Schirok, *J. Am. Chem. Soc.* **1999**, *121*, 10264–10269.

[43] M. Kitamura, S. Zaman, K. Narasaka, *Synlett* **2001**, 974–976; S. M. Zaman, K. Kitamura, K. Narasaka, *Bull. Chem. Soc. Jpn.* **2003**, *76*, 1055–1062.

[44] M. Kitamura, S. Chiba, O. Saku, K. Narasaka, *Chem. Lett.* **2002**, 606–607; S. Chiba, M. Kitamura, O. Saku, K. Narasaka, *Bull. Chem. Soc. Jpn.* **2004**, *77*, 785–796.

[45] S. Nishimura, T. Uemura, *J. Am. Chem. Soc.* **2000**, *122*, 12049–12050; T. Nishimura, Y. Nishiguchi, Y. Maeda, S. Uemura, *J. Org. Chem.* **2004**, *69*, 5342–5347.

Received: June 1, 2005