JOC Article

Palladium-Catalyzed Transformation of Cyclobutanone *O*-Benzoyloximes to Nitriles via C−C Bond Cleavage

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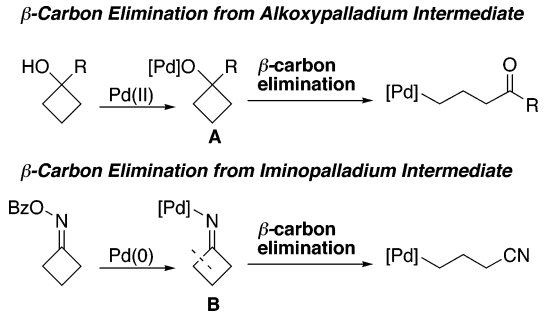
Palladium-catalyzed transformation of cyclobutanone *O*-benzoyloximes to a variety of nitriles is described. The reaction may proceed via two important steps, that is, (i) oxidative addition of the N−O bond of oximes to Pd(0) to give a cyclobutylideneaminopalladium(II) species and (ii) β-carbon elimination of this species to afford a reactive alkylpalladium species. The kind of products is very dependent on the nature of substituents on the cyclobutane ring. The direction of the C−C bond cleavage is controlled by the kind of ligand employed. The sequential reaction composed of the C−C bond cleavage and the subsequent intra- and intermolecular C−C bond formations via the corresponding alkylpalladium species is also demonstrated. For example, an oxime having an alkynyl moiety at a suitable position reacts with a variety of alkenes to afford nitriles bearing dienylcyclopentane moiety in moderate to good yields.

Introduction

We have so far developed a novel Pd catalytic system, which affords ketones from cyclobutanols via C−C bond cleavage (Scheme 1). The system involves β-carbon elimination[1,2] from an intermediate palladium(II)-alcoholate (**A**), where the strain release from cyclobutane ring is a driving force.[3] Similar β-carbon elimination is expected to occur to give nitriles if a cyclobutylideneaminopalladium(II) species such as **B** is formed as an intermediate by oxidative addition of the N−O bond to Pd(0) in the reaction with cyclobutanone oximes (Scheme 1).

More specifically, β-carbon elimination from an intermediate **B′** might give a γ-cyanoalkylpalladium species (**C**), the formation of which leads to several nitriles depending on the kind of substituents R′ and R″ via depalladation (Scheme 2). The step of oxidative addition of ketone *O*-acyloximes to Pd(0) to afford such an alkylideneaminopalladium(II) species has been postulated by Narasaka and co-workers in the synthesis of heterocyclic compounds from the oximes.[4,5] Their work prompted us to develop a new method for the synthesis of nitriles involving two unique steps, namely, oxidative addition of the N−O bond giving **B′** followed by β-carbon elimination to afford **C**. In this article we describe the results of the palladium(0)-catalyzed intra- and intermolecular reactions of cyclobutanone *O*-benzoyloximes having various kinds of substituents on cyclobutane ring leading to a variety of nitriles.[6,7]

SCHEME 1



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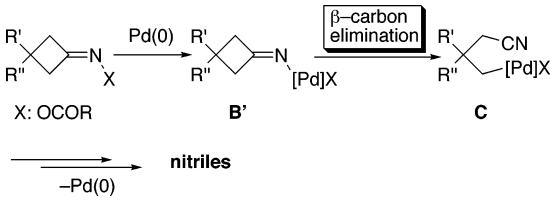


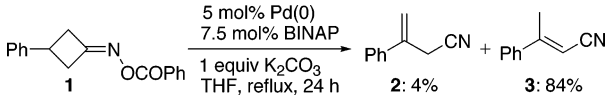
(1) (a) Nishimura, T.; Ohe, K.; Uemura, S. *J. Am. Chem. Soc.* **1999**, *121*, 2645. (b) Nishimura, T.; Ohe, K.; Uemura, S. *J. Org. Chem.* **2001**, *66*, 1455. (c) Nishimura, T.; Uemura, S. *J. Am. Chem. Soc.* **1999**, *121*, 11010. (d) Nishimura, T.; Matsumura, S.; Maeda, Y.; Uemura, S. *Chem. Commun.* **2002**, 50. (e) Nishimura, T.; Matsumura, S.; Maeda, Y.; Uemura, S. *Tetrahedron Lett.* **2002**, *43*, 3037. (f) Matsumura, S.; Maeda, Y.; Nishimura, T.; Uemura, S. *J. Am. Chem. Soc.* **2003**, *125*, 8862. (g) Nishimura, T.; Araki, H.; Maeda, Y.; Uemura, S. *Org. Lett.* **2003**, *5*, 2997.

(2) For examples of the reaction involving β-carbon elimination from transition metal alcoholates, see: (a) Harayama, H.; Kuroki, T.; Kimura, M.; Tanaka, S.; Tamaru, Y. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2352. (b) Kondo, T.; Kodoi, K.; Nishinaga, E.; Okada, T.; Morisaki, Y.; Watanabe, Y.; Mitsudo, T. *J. Am. Chem. Soc.* **1998**, *120*, 5587. (c) Park, S.-B.; Cha, J. K. *Org. Lett.* **2000**, *2*, 147. (d) Okumoto, H.; Jinnai, T.; Shimizu, H.; Harada, Y.; Mishima, H.; Suzuki, A. *Synlett* **2000**, 629. (e) Terao, Y.; Wakui, H.; Satoh, T.; Miura, M.; Nomura, M. *J. Am. Chem. Soc.* **2001**, *123*, 10407. (f) Terao, Y.; Wakui, H.; Nomoto, M.; Satoh, T.; Miura, M.; Nomura, M. *J. Org. Chem.* **2003**, *68*, 5236.

(3) For reviews of the reaction of small ring compounds, see: (a) Small Ring Compounds in Organic Synthesis I−IV. In *Topics in Current Chemistry*; de Meijere, A., Ed.; Springer-Verlag: Berlin, 1986 (Vol. 133); 1987 (Vol. 135); 1988 (Vol. 144); 1990 (Vol. 155). (b) Durst, T.; Breau, L. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, U.K., 1991; Vol. 5, pp 675−697. (c) Hudlicky, T.; Reed, J. W. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, U.K., 1991; Vol. 5, pp 899−970. (d) Piers, E. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, U.K., 1991; Vol. 5, pp 971−998. (e) Bronson, J. J.; Danheiser, R. L. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, U.K., 1991; Vol. 5, pp 999−1035.

10.1021/jo049385k CCC: $27.50
Published on Web 07/02/2004

SCHEME 3



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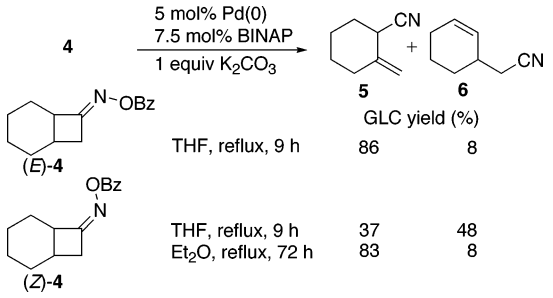


Results and Discussion

Formation of Nitriles Having Carbon−Carbon Unsaturated Bonds. The first attempt to prepare nitriles from 3-phenylcyclobutanone *O*-benzoyloxime (**1**) via C−C bond cleavage was carried out in the presence of a palladium(0) catalyst, 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (BINAP), and K_2CO_3 in tetrahydrofuran (THF) (Scheme 3).[6] The major product was the α,β-unsaturated nitrile **3** in this case.

The interesting selectivity was observed when *O*-benzoyloxime **4** was used as a substrate.Thus, its (*E*)-isomer (*E*)-**4** afforded the nitrile **5** as a major product in 86% yield together with 8% of the nitrile **6**, while (*Z*)-**4** (*Z*-isomer) gave **5** and **6** in 37% and 48% yields, respectively (Scheme 4). When the reaction of (*Z*)-**4** was carried out at lower temperature (in diethyl ether at reflux), **5** became the main product (83%).

The plausible pathway for the formation of these products is shown in Scheme 5. The oxidative addition of the N−O bond of (*E*)-**4** occurs to give an alkylideneaminopalladium species *E*-**I**,[8] and successive β-carbon syn-elimination followed by β-hydrogen elimination affords the nitrile **5** as a major product. On the other hand, (*Z*)-**4** gives *Z*-**I**, which leads to the nitrile **6** via similar elimination. In the case of (*Z*)-**4**, the formation of **5** implies that an isomerization of *Z*-**I** to *E*-**I** occurs during the reaction, since the *E*/*Z*-isomerization of **4** was not observed at all in the absence of a Pd(0) catalyst.

SCHEME 5

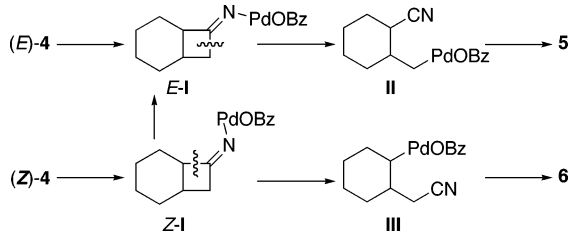
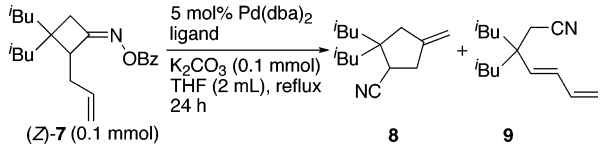


TABLE 1. Effect of Ligands in the Reaction of (*Z*)-7



entry	ligand (mol %)	GLC yield (**8** + **9**,%)	ratio (**8**/**9**)[a]
1	(*R*)-BINAP (7.5)	63	25/75
2[b]	(*R*)-BINAP (7.5)	88	25/75
3	(*R*)-MeO-MOP (20)	82	19/81
4	(*S*)-H-MOP (20)	82	49/51
5	PPh_3[c]	39	57/43
6	PCy_3 (10)	51	75/25
7	(*R*)-(*S*)-PPFA (10)	15	28/72
8	(*R*)-(*S*)-PPFCyA (10)	74	84/16
9	(*R*)-(*S*)-PPFAdA (10)	47	70/30

[a] Determined by GLC. [b] For 39 h. [c] 5 mol % $Pd(PPh_3)_4$ was used.

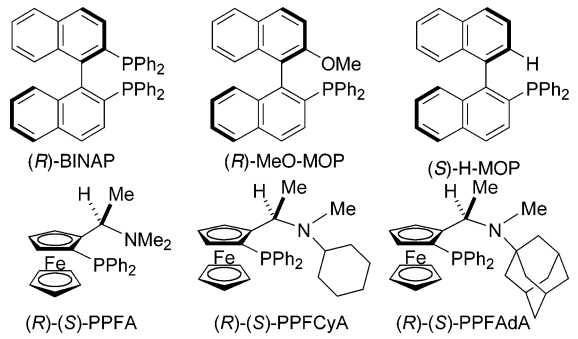


FIGURE 1.

According to the results described above, the C−C bond cleavage generally favors the formation of a sterically less hindered primary alkylpalladium species. It was also observed that the direction of the C−C bond cleavage was affected by the configuration of the isomers (*E*) or (*Z*) in some extent. To investigate how the selectivity of direction of the C−C bond cleavage is affected by a kind of ligand, 3,3-diisobutyl-2-allylcyclobutanone *O*-benzoyloxime (**7**) was treated in the presence of Pd(0) catalyst and a phosphine ligand. Treatment of (*Z*)-**7** in the presence of $Pd(dba)_2$, (*R*)-BINAP, and K_2CO_3 in THF at 90 °C gave nitriles **8** and **9** in 88% yield (**8**/**9** = 25/75, Table 1, entries 1 and 2). The reaction using MeO-MOP[9] as a ligand also gave **9** preferentially (entry 3). On the other hand, when the reaction was carried out with ligands such as PCy_3, PPFCyA, and PPFAdA (Figure 1),[1f] the nitrile **8** was obtained as a major product (entries 6, 8, and 9).

The formation of two products is explained as shown in Scheme 6. First, oxidative addition of the N−O bond

(4) (a) Tsutsui, H.; Narasaka, K. *Chem. Lett.* **1999**, 45. (b) Tsutsui, H.; Narasaka, K. *Chem. Lett.* **2001**, 526. (c) Kitamura, M.; Zaman, S.; Narasaka, K. *Synlett* **2001**, 974. (d) Kitamura, M.; Chiba, S.; Saku, O.; Narasaka, K. *Chem. Lett.* **2002**, 606. (e) Narasaka, K. *Pure Appl. Chem.* **2002**, *74*, 143. (f) Tsutsui, H.; Kitamura, M.; Narasaka, K. *Bull. Chem. Soc. Jpn.* **2002**, *75*, 1451. (g) Kitamura, M.; Narasaka, K. *Chem. Rec.* **2002**, *2*, 268. (h) Zaman, S.; Kitamura, M.; Narasaka, K. *Bull. Chem. Soc. Jpn.* **2003**, *76*, 1055.

(5) For examples of oxidative addition of oximes to metal, see: (a) Deeming, A. J.; Owen, D. W.; Powell, N. I. *J. Organomet. Chem.* **1990**, *398*, 299. (b) Ferreira, C. M. P.; Guedes da Silva, M. F. C.; Kukushkin, V. Y.; Fraúo da Silva, J. J. R.; Pombeiro, A. J. L. *J. Chem. Soc., Dalton Trans.* **1998**, 325.

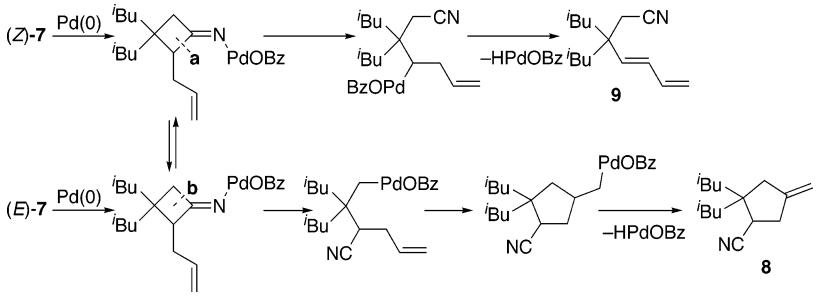
(6) (a) Nishimura, T.; Uemura, S. *J. Am. Chem. Soc.* **2000**, *122*, 12049. (b) Nishimura, T.; Uemura, S. *Synlett* **2004**, 201.

(7) For examples of palladium-induced Beckmann fission of oximes to give nitriles, see: (a) Maeda, K.; Moritani, I.; Hosokawa, T.; Murahashi, S.-I. *J. Chem. Soc., Chem. Commun.* **1975**, 689. (b) Leusink, A. J.; Meerbeek, T. G.; Noltes, J. G. *Recl. Trav. Chim. Pays-Bas* **1976**, *95*, 123.

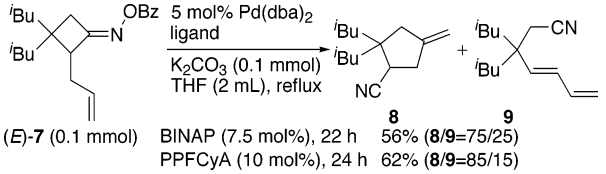
(8) For an example of the isolation of *N*-metalloimine complex containing Re, see: Hevia, E.; Pérez, J.; Riera, V.; Miguel, D. *Angew. Chem., Int. Ed.* **2002**, *41*, 3858.

(9) (a) Uozumi, Y.; Hayashi, T. *J. Am. Chem. Soc.* **1991**, *113*, 9887. (b) Uozumi, Y., Suzuki, N., Ogiwara, A.; Hayashi, T. *Tetrahedron* **1994**, *50*, 4293.

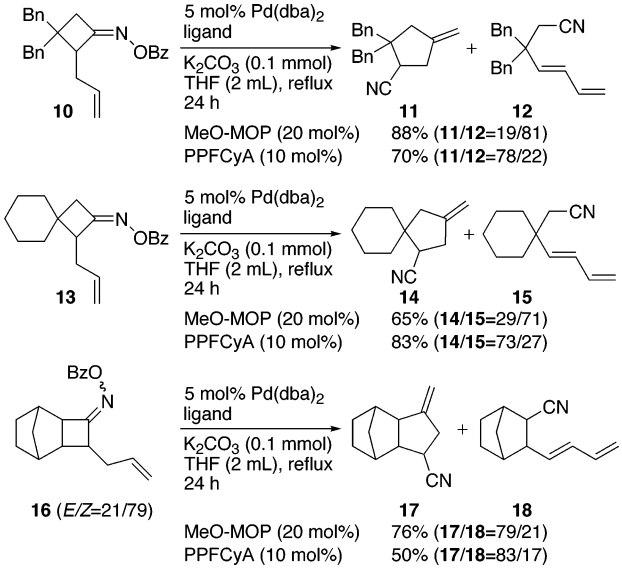
SCHEME 6



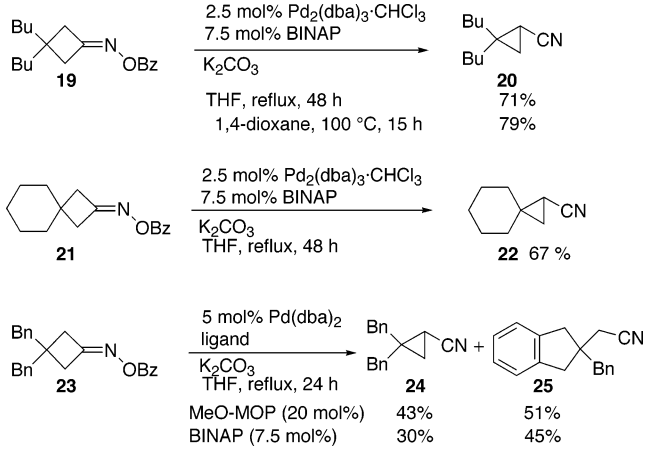
SCHEME 7



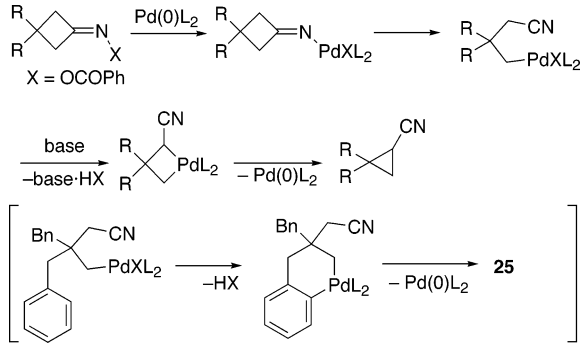
SCHEME 8



SCHEME 9



SCHEME 10



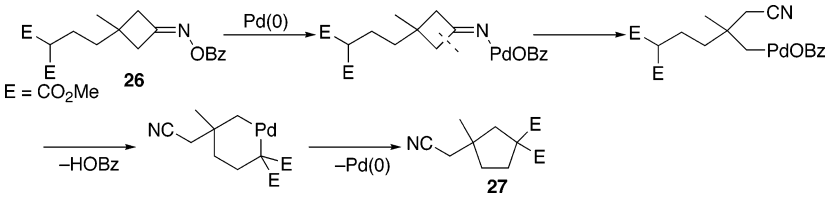
of (*Z*)-**7** to Pd(0) occurs to give a (*Z*)-alkylideneaminopalladium species. Then, the C−C bond **a** is cleaved to afford a secondary-alkylpalladium species, and the nitrile **9** is produced by the successive *β*-hydrogen elimination. On the other hand, the (*Z*)-alkylideneaminopalladium species isomerizes to the (*E*)-isomer, which affords a sterically less hindered primary-alkylpalladium species. The species undergoes intramolecular cyclization with alkenic moiety followed by *β*-hydrogen elimination to afford the nitrile **8**.

The direction of the C−C bond cleavage is controlled by the configuration of oximes (*E* or *Z*) in the reaction using ligands such as BINAP and MOPs, while the use of PCy_3, PPFCyA, and PPFAdA makes the C−C bond cleave to afford the sterically less hindered primary-alkylpalladium species from both (*E*)- and (*Z*)-oximes. These observations are consistent with the result of the reaction of (*E*)-**7** in the use of BINAP as a ligand, where the nitrile **8** was obtained as a major product opposite to the result of (*Z*)-**7** case (Scheme 7).

Similar reactivity was also observed in the reaction of other oximes such as **10**, **13**, and **16**, all of which afforded the corresponding nitriles in moderate to good yields (Scheme 8).

Formation of Cyclopropanecarbonitriles. Cyclobutanone *O*-benzoyloximes such as **19** and **21** having no hydrogen available to be eliminated after the formation of an alkylpalladium intermediate afforded cyclopropanecarbonitriles via an intramolecular cyclization (Scheme 9). For example, cyclopropanecarbonitriles **20** and **22** were obtained from oximes **19** and **21** in 79% and 67% yields, respectively. 3,3-Dibenzylcyclobutanone *O*-benzoyloxime (**23**) produced a mixture of cyclopropanecarbonitrile **24** and a nitrile having indane framework **25** in good yields. The formation of these cyclopropanes may be explained by the reaction pathway shown in Scheme 10. Thus, an intramolecular attack of an active methylene carbon of an intermediate alkylpalladium benzoate species to the palladium in the presence of a base affords a palladacyclobutane, the reductive elimination of Pd(0) species from which gives the products. The nitrile **25** might be formed via an intramolecular C−H activation[10]

SCHEME 11



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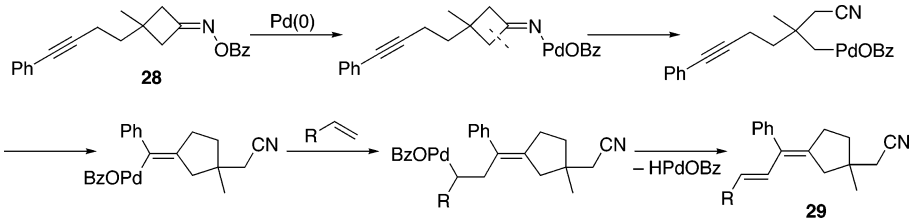
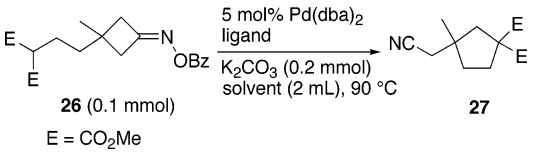


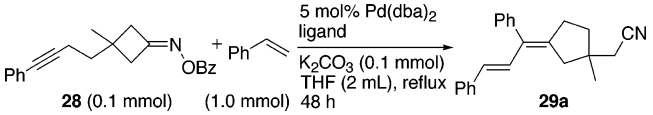
TABLE 2. Effect of Ligands in the Reaction of 26



entry	ligand (mol %)	solvent	time (h)	GLC yield (%)
1[a]	(*R*)-BINAP (7.5)	THF	72	12
2	(*R*)-MeO-MOP (20)	THF	48	21
3	(*R*)-MeO-MOP (20)	DME	24	31
4	(*R*)-BINAP (7.5)	DME	24	27
5	PPFCyA (10)	DME	24	5

[a] K_2CO_3 (0.1 mmol) was used. DME = 1,2-dimethoxyethane

TABLE 3. Effect of Ligands in the Reaction of 28 with Styrene



entry	ligand (mol %)	isolated yield of **29** (%)
1	PCy_3 (10)	0
2[a]	PPh_3 (10)	tr
3	dppe (7.5)	0
4	dppb (7.5)	tr
5	PPFCyA (10)	tr
6	dppf (7.5)	24
7	(*R*)-MeO-MOP (20)	57
8	(*R*)-BINAP (7.5)	75

[a] $Pd(PPh_3)_4$ (5 mol %) was used.

at benzene ring in an alkylpalladium intermediate formed by β-carbon elimination.

Formation of Nitriles Having a Cyclopentane Framework. Several methods for the transformation of an alkylpalladium species have so far been established.[11] Especially, the C−C bond formation is useful to construct the target organic molecules.[12] It was expected that the oxime **26** having a nucleophilic carbon center might afford cyclopentane derivatives via an intramolecular cyclization of an alkylpalladium intermediate formed from an alkylideneaminopalladium species by β-carbon elimination (Scheme 11). Thus, we prepared the oxime **26** and carried out its Pd(0)-catalyzed reaction. Although several reaction conditions were tested to obtain the desired product, the product yield was low, unfortunately, as summarized in Table 2.

As the product nitrile **27** has a chiral carbon center, it might be possible to obtain the optically active nitrile if the enantioselective C−C bond cleavage could occur from the chiral ligands-ligated aminopalladium species. No asymmetric induction, however, was actually observed in this reaction despite the use of several chiral ligands.

Next, the oxime **28**, which has an alkynyl moiety in the molecule, was prepared. This compound is expected to give a vinylpalladium species via β-carbon elimination followed by an intramolecular palladation. The species may undergo a Mizoroki−Heck type of reaction to afford a new C−C bond-forming product if alkenes were present in the system (Scheme 12).[13]

First, the reaction of the oxime **28** with styrene was examined in the presence of $Pd(dba)_2$, a phosphine ligand, and K_2CO_3 in refluxing THF (bath temp 90 °C) for 48 h (Table 3). Phosphine ligands such as PCy_3, PPh_3, dppe, dppb, and PPFCyA were not effective for this reaction (entries 1−5). The desired product **29a** was obtained when such ligands as dppf, MeO-MOP, and BINAP were employed in which BINAP was most effective to give **29a** in 75% yield (entry 8). Next, the effect of solvents was investigated using BINAP as a ligand (Table 4). Among solvents, aprotic polar solvents such as DMF (*N*,*N*-dimethylformamide) and DMA (*N*,*N*-dimethylacetoamide) were revealed to be more effective than THF, 1,4-dioxane, NMP (*N*-methylpyrrolidinone), and toluene to give **29a** in 83% and 82% yields, respectively (Table 4, entries 6 and 8).

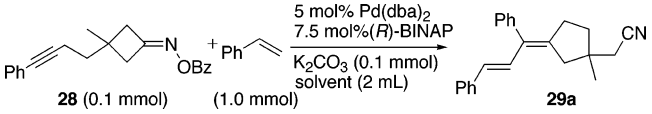
(10) For recent reviews, see: (a) Shilov, A. E.; Shul'pin, G. B. *Chem. Rev.* **1997**, *97*, 2879. (b) Dyker, G. *Angew., Chem. Int. Ed.* **1999**, *38*, 1698. (c) Kakiuchi, F.; Murai, S. *Acc. Chem. Res.* **2002**, *35*, 826. (d) Ritleng, V.; Sirlin, C.; Pfeffer, M. *Chem. Rev.* **2002**, *102*, 1731.

(11) Tsuji, J. *Palladium Reagents and Catalysis; Innovations in Organic Synthesis*; Wiley: New York, 1995.

(12) For example, see: Grigg, R.; Sridharan, V. *J. Organomet. Chem.* **1999**, *576*, 65.

(13) For recent reviews of domino reaction using a palladium catalyst, see: (a) de Meijere, A.; Bräse S. *J. Organomet. Chem.* **1999**, *576*, 88. (b) Poli, G.; Giambastiani, G.; Heumann, A. *Tetrahedron* **2000**, *56*, 5959.

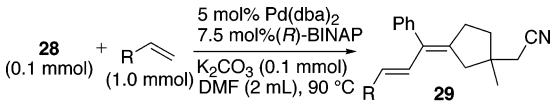
TABLE 4. Effect of Solvents in the Reaction of 28 with Styrene

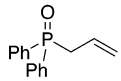


entry	solvent	bath temp (°C)	time (h)	isolated yield (%)
1	THF	90	48	75
2[a]	THF	90	48	5
3	toluene	90	40	29
4	toluene	120	13	40
5	1,4-dioxane	120	19	57
6	DMF	90	15	83
7[b]	DMF	90	8	59
8	DMA	90	15	82
9	NMP	90	15	56

[a] Styrene (0.2 mmol) was used. [b] DMF (0.5 mL) was used.

TABLE 5. Reactions of 28 with Alkenes



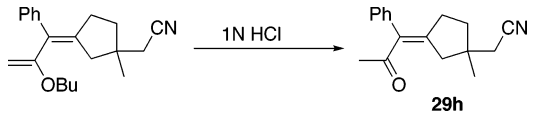
entry	alkene	time (h)	product	isolated yield (%)
1	4-ClC$_6$H$_4$	24	**29b**	72
2	C$_6$H$_{13}$	19	**29c**	67
3		72		15
4[a]	^{t}Bu	72	**29d**	26
5[b]		69		33
6	Me$_3$Si	15	**29e**	68
7[a]		15		73
8		18	**29f**	50
9[c]	EtCO$_2$	72	**29g**	55
10	BuO	12	**29h**	26[d]
11[a]		18		43[d]

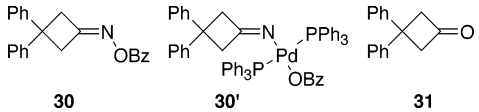
[a] Alkene (2.0 mmol) was used. [b] Alkene (3.0 mmol) was used. [c] In THF at reflux. [d] Yield after hydrolysis.

The product **29a** has a chiral carbon center, but no asymmetric induction was observed under the reaction conditions. The reaction of the oxime **28** with several other alkenes in DMF was also carried out, and typical results are shown in Table 5. The use of *p*-chlorostyrene and 1-octene gave the corresponding nitriles **29b** and **29c** in 72% and 67% yields, respectively (entries 1 and 2). The reaction of **28** with 3,3-dimethyl-1-butene was very slow, and the product yield was low (entries 3−5), whereas trimethylvinylsilane and allyldiphenylphosphine oxide gave the corresponding nitriles in moderate to good yields (entries 6−8). Ethyl acrylate also afforded **29g** in 55% yield after 72 h in refluxing THF. In the case of an electron-rich alkene, such as butyl vinyl ether, a normal selectivity of the direction of alkene insertion was observed[11] and α,β-unsaturated ketone **29h** was obtained after hydrolysis of the initial product (Scheme 13).

Stoichiometric Reaction of 3,3-Diphenylcyclobutanone *O*-Benzoyloxime with Pd(PPh$_3$)$_4$: Attempt to Isolate an Intermediate. It is assumed that whole reactions of cyclobutanone *O*-benzoyloximes described above are initiated by the oxidative addition of N−O bond to Pd(0). This step was first proposed by Narasaka and co-workers in the transformation of γ,δ-unsaturated ketone *O*-pentafluorobenzoyloximes to pyrrole derivatives. They detected the formation of some palladium complexes in the reaction of Pd(PPh$_3$)$_4$ with 4,4′-bis(trifluoromethyl)benzophenone *O*-methylsulfonyloxime by ^{31}P NMR spectroscopy.[4f] To confirm the presence of an intermediate alkylideneaminopalladium species in our reaction system, we tried to isolate the oxidative addition product of 3,3-diphenylcyclobutanone *O*-benzoyloxime **30** to Pd(PPh$_3$)$_4$. An equimolar mixture of **30** and Pd(PPh$_3$)$_4$ was stirred in THF at 50 °C. After 4 h, the complete conversion of **30** was detected by TLC analysis. After concentration of the reaction mixture, a resulting yellow solid was collected by filtration and washed with diethyl ether. By the measurement of ^{1}H NMR of this solid, however, the peaks of the methylene protons of cyclobutane ring could not be observed at around δ 3−4 ppm [at 3.89 ppm (br s, 4H, in CDCl$_3$) for methylene protons of **30**], suggesting that the yellow solid was not the desired complex **30′**.[14] Then, we monitored the stoichiometric reaction between **30** and Pd(PPh$_3$)$_4$ by ^{1}H and ^{31}P NMR spectroscopy. First, the reaction in benzene-d_6 in an NMR tube at 25 °C was monitored by ^{1}H NMR. As a result, the peaks (3.33−3.41 ppm, 4H) for methylene protons of **30** were gradually disappeared, while new peaks at 3.32, 3.53, and 2.93 ppm appeared. The singlet peak at 3.32 ppm could be assigned as 3,3-diphenylcyclobutanone (**31**). After 23 h, the mixture was heated at 50 °C for 1 h, resulting in the increase of the formation of **31**. The measurement of ^{31}P NMR on this reaction at 25 °C in THF-d_8 showed new peaks at 29.5, 22.7, and 14.7 ppm after 2 h. After heating at 50 °C for 1 h, only two peaks at 22.7 and 21.0 ppm were observed. These results suggest that an intermediate produced in the reaction of the benzoyloxime with Pd(PPh$_3$)$_4$ is not stable enough to be detected even by NMR and decomposes to the ketone **31** as a result of the hydrolysis by a small amount of water contained in a solvent.[4a] Next, benzoyloximes **32** and **34** were treated under our reaction conditions as shown in Scheme 14, the latter of which are known to afford the pyrrole **33** under Narasaka's conditions.[4] In fact, the pyrrole **33** was also obtained in both reactions under our reaction conditions, although the yields were low. These results suggest that an alkylideneaminopalladium species is also formed in our case, although the exact structure of it could not be determined at the present stage.

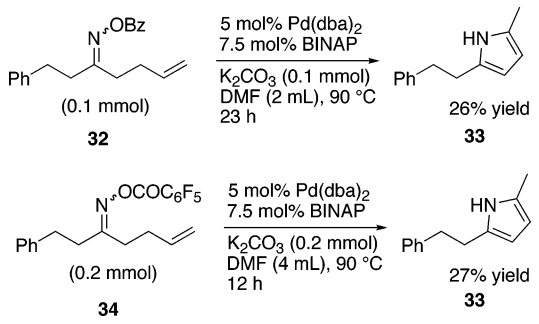
SCHEME 13





(14) The yellow solid might be a palladium complex such as Pd(PPh$_3$)$_n$.

SCHEME 14



Conclusion

Novel transformations of cyclobutanone *O*-benzoyloximes to nitriles via a C−C bond cleavage by palladium catalysis have been demonstrated where the direction of the C−C bond cleavage was very dependent on the kind of phosphine ligands employed. The reaction seems to proceed via oxidative addition of the N−O bond to Pd(0) to afford an alkylideneaminopalladium intermediate followed by β-carbon elimination. The sequential reaction composed of the C−C bond cleavage and the subsequent intra- and intermolecular C−C bond formations via the corresponding alkylpalladium species have also been demonstrated to construct a variety of nitrile derivatives. The findings disclosed here afford the new methodology for nitrile synthesis.

Experimental Section

General Method. ^{1}H NMR spectra were obtained in $CDCl_3$ or C_6D_6 at 300 or 400 MHz with Me_4Si as an internal standard. ^{13}C NMR spectra were obtained at 75.5 or 100 MHz. ^{31}P NMR spectra were obtained at 161.9 MHz.

Materials. Commercially available organic and inorganic compounds were used without further purification except for solvent, which was distilled by the known method before use.[15] $Pd(dba)_2$ (dba = dibenzylideneacetone) was synthesized by the literature method.[16] Cyclobutanone *O*-benzoyloximes were prepared according to the reported procedures from the corresponding cyclobutanone oximes.[4f] Cyclobutanones were obtained from the reduction of 2,2-dichlorocyclobutanones, which were prepared from the corresponding alkenes and trichloroacetyl chloride.[17] (*R*)-MeO-MOP and (*S*)-H-MOP[9] were prepared according to the reported procedures.

Typical Procedure for Reaction of Cyclobutanone *O*-Benzoyloximes (1, 4, 19, 21, 23). To a mixture of $Pd_2(dba)_3$·$CHCl_3$ (0.0125 mmol), (*R*)-(+)-BINAP (0.0375 mmol), and THF (2 mL) in a 10-mL two-necked flask were added K_2CO_3 (0.50 mmol), cyclobutanone *O*-benzoyloxime (0.50 mmol), and THF (3 mL) under N_2, and the mixture was stirred at 90 °C (bath temp) until the reaction had reached completion by monitoring with TLC analysis. The reaction mixture was cooled to room temperature and then filtered through a pad of Florisil. The filtrate was concentrated under vacuum to give a yellow oil, which was subjected to column chromatography on SiO_2 with diethyl ether−hexane (4/96) as an eluent. All major products were isolated and identified by ^{1}H and ^{13}C NMR, IR, and C, H, N combustion analysis.

Typical Procedure for Reaction of Cyclobutanone *O*-Benzoyloximes (7, 10, 13, 16, 23). To a mixture of $Pd(dba)_2$ (0.005 mmol), (*R*)-MeO-MOP(0.02 mmol) or (*R*)-*N*-cyclohexyl-*N*-methyl-1-[(*S*)-2-(diphenylphosphino)ferrocenyl]-ethylamine (0.01 mmol), K_2CO_3 (0.10 mmol), and THF (0.5 mL) were added allyl-substituted cyclobutanone *O*-benzoyloxime (0.10 mmol) and THF (1.5 mL) under N_2, and the mixture was stirred at 90 °C (bath temp) for 24 h. After completion of the reaction, the reaction mixture was cooled to room temperature and then filtered through a pad of Florisil. The filtrate was concentrated under vacuum to give a yellow oil, which was subjected to column chromatography on SiO_2. All major products were isolated and identified by ^{1}H and ^{13}C NMR and C, H, N combustion analysis or mass spectroscopy.

Typical Procedure for Reaction of 26. The procedure of the reaction of the compound **26** was the same as that of the reaction of allyl-substituted cyclobutanone *O*-benzoyloximes. The yield of the compound **27** was determined by GLC using pentamethylbenzene as an internal standard.

Typical Procedure for Reaction of 28 with Alkenes. To a mixture of $Pd(dba)_2$ (0.0050 mmol), (*R*)-(+)-BINAP (0.0075 mmol), K_2CO_3 (0.10 mmol), and DMF (0.5 mL) were added alkene (1.0 mmol), **28** (0.10 mmol) and DMF (1.5 mL) under N_2, and the resulting mixture was stirred at 90 °C until the reaction completed. After completion of the reaction, the reaction mixture was cooled to room temperature and then filtered through a pad of Florisil. The filtrate was concentrated under vacuum to give a yellow oil, which was subjected to column chromatography on SiO_2. All major products were isolated and identified by ^{1}H and ^{13}C NMR and C, H, N combustion analysis or mass spectroscopy.

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Supporting Information Available: Experimental procedure and characterization data for all compounds and X-ray crystal structure of **29f** (CIF format). This material is available free of charge via the Internet at http://pubs.acs.org.

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