Palladium-Catalyzed Carbonylative [2 + 2] Cycloaddition for the Stereoselective Synthesis of Either *cis*- or *trans*-3-Alkenyl β-Lactams

Hideo Tanaka, A. K. M. Abdul Hai, Masahiro Sadakane, Hiroshi Okumoto, and Sigeru Torii*

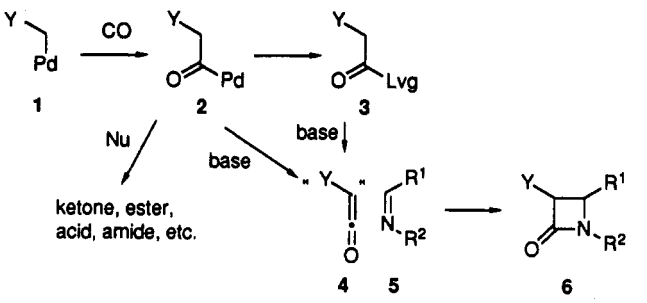
Department of Applied Chemistry, Faculty of Engineering, Okayama University, Tsushima-Naka, Okayama 700, Japan

Received September 7, 1993 (Revised Manuscript Received March 21, 1994•)

A new potential alkenylketene equivalent, prepared without use of a carboxylic acid or an activated derivative, has been exploited. Palladium-catalyzed carbonylation of an allyl phosphate in the presence of an imine and a tertiary amine under CO pressure (30 kg cm^{-2}) stereoselectively gave either a *cis*- or *trans*-3-alkenyl β-lactam in high yield. The stereochemical outcome strongly depends on the nature of the imine employed. Imines conjugated with a carbonyl such as a ketone or an ester stereoselectively produce *cis*-β-lactams at room temperature, whereas imines unconjugated with a carbonyl group exclusively afford *trans*-β-lactams at 70 °C.

The recent significant development of direct catalytic routes to carbonyl-containing compounds using CO as the carbonyl source has resulted in the expanded use of the catalytic carbonylation.[1] In particular, Pd-catalyzed carbonylation has provided an efficient tool for the construction of such molecules.[2] An enormous amount of work has been done on the reactivity of acylpalladium complexes, through which many new and potentially useful reactions have been developed. In the course of our research on carbonylation processes using Pd catalysts,[3] we noticed the diverse utility of intermediary acyl complexes **2** as illustrated in Scheme 1. For instance, it is well documented that acylpalladium **2**, formed by CO insertion into alkylpalladium **1**, reacts with various nucleophiles to give ketones, acids, esters, and amides.[1,2] The similarity between these acylpalladiums and acid chlorides suggested that activated acyl analogues **2** could serve as precursors for ketene **4** or its equivalents.[4] Since the α-proton of **2** is acidic enough to be deprotonated by a weak base, displacement of the Pd atom of complex **2** with an appropriate nucleophile, which could in turn become a good leaving group, could lead to activated carboxylic acid derivatives **3**. If the carbonylation could provide a ketene or an equivalent, the great diversity of acylpalladiums would open a new route to ketene-mediated organic syntheses.

Scheme 1



The most prominent use of ketenes is for [2 + 2] cycloadditions with imines for the construction of the β-lactam skeleton.[5] The importance of carbapenams bearing a hydroxyalkyl group at the 3-position led us to study the carbonylation of π-allylpalladium species. Numerous allylic alcohol derivatives,[2] among them carbonates[6] and phosphates,[7] have been demonstrated to undergo Pd-catalyzed carbonylation via π-allylpalladium species under mild conditions. The expected product of carbonylative [2 + 2] cycloaddition would possess an alkenyl appendage at the appropriate position, which could be readily converted into the desired substituents. Hence, the allylic compounds were anticipated to be convenient candidates for ketene precursors leading to 3-alkenyl β-lactams, which were intriguing enough for us to study the Pd-catalyzed carbonylative [2 + 2] cycloadditions with imines. The conventional methods for the generation of ketenes require the activation of a carboxylic acid by treatment with chlorinating agents,[5a] DCC,[8] cyanuric acid,[9] or dichlorophosphate,[10] and then the activated substances have to be exposed to a base. This cumbersome procedure and the necessity for activating agents sometimes decrease

• Abstract published in *Advance ACS Abstracts*, May 1, 1994.

(1) Colquhoun, H. M.; Thompson, D. J.; Twigg, M. V. *Carbonylation*; Plenum Press: New York, 1991.

(2) Tsuji, J. *Organic Synthesis with Palladium Compounds*; Springer Verlag: Berlin, 1980. Heck, R. F. *Palladium Reagents in Organic Syntheses*; Academic Press: London, 1985.

(3) Torii, S.; Okumoto, H.; Xu, L. H. *Tetrahedron Lett.* **1990**, *31*, 7175–7178. Torii, S.; Okumoto, H.; Xu, L. H. *Tetrahedron Lett.* **1991**, *32*, 237–240. Torii, S.; Xu, L. H.; Okumoto, H. *Synlett* **1991**, 695–696. Torii, S.; Xu, L. H.; Sadakane, M.; Okumoto, H. *Synlett* **1992**, 513–514.

(4) For the late transition metal promoted ketene formation, see; (a) Ogoshi, S.; Ohe, K.; Chatani, N.; Kurosawa, H.; Murai, S. *Organometallics* **1991**, *10*, 3813–3818. (b) Miyashita, A.; Kawashima, T.; Kaji, S.; Nomura, K.; Nohira, H. *Tetrahedron Lett.* **1991**, *32*, 781–784. (c) Iwasaki, M.; Kobayashi, Y.; Li, J.; Matsuzaka, H.; Ishii, Y.; Hidai, M. *J. Org. Chem.* **1991**, *56*, 1922–1927. (d) Wouters, J. M. A.; Avis, M. W.; Elsevier, C. J.; Kyriakidis, C. E.; Stam, C. H. *Organometallics* **1990**, *9*, 2203–2205. (e) Huser, M.; Youinou, M.; Osborn, J. A. *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 1386–1388. (f) Miyashita, A.; Nomura, K.; Kaji, S.; Nohira, H. *Chem. Lett.* **1989**, 1983–1986. (g) Miyashita, A.; Kihara, T.; Nomura, K.; Nohira, H. *Chem. Lett.* **1986**, 1607–1610. (h) Hommeltoft, S. I.; Baird, M. C. *Organometallics* **1986**, *5*, 190–195. (i) Bodnar, T. W.; Crawford, E. J.; Cutler, A. R. *Organometallics* **1986**, *5*, 947–950. (j) Miyashita, A.; Shitara, H.; Nohira, H. *Organometallics* **1985**, *4*, 1463–1464. (k) Hommeltoft, S. I.; Baird, M. C. *J. Am. Chem. Soc.* **1985**, *107*, 2548–2549. (l) Herrmann, W. A.; Plank, J.; Ziegler, M. L.; Weidenhammer, K. *J. Am. Chem. Soc.* **1979**, *101*, 3133–3135. and references cited therein.

(5) (a) Thomas, R. C. in *Recent Progress in the Chemical Synthesis of Antibiotics*; Lukacs, G.; Ohno, M. Eds.; Springer Verlag: Berlin, 1990, 534–564. Palomo, C. *ibid.*, 565–612. (b) Carruthers, W. *Cycloaddition Reactions in Organic Synthesis*; Pergamon Press: Oxford, 1990, 332–367.

(6) Tsuji, J.; Sato, K.; Okumoto, H. *J. Org. Chem.* **1984**, *49*, 1341–1344. Tsuji, J.; Sato, K.; Okumoto, H. *Tetrahedron Lett.* **1982**, *23*, 5189–5190.

(7) Murahashi, S.; Imada, Y.; Taniguchi, Y.; Higashiura, S. *J. Org. Chem.* **1993**, *58*, 1538–1545. Murahashi, S.; Imada, Y.; Taniguchi, Y.; Higashiura, S. *Tetrahedron Lett.* **1988**, *29*, 4945–4948.

(8) Olah, G. A.; Wu, A.; Farooq, O. *Synthesis* **1989**, 568–568.

(9) Manhas, M. S.; Bose, A. K.; Khajavi, M. S. *Synthesis* **1981**, 209–211.

(10) Arrieta, A.; Cossio, F. P.; Palomo, C. *Tetrahedron* **1985**, *41*, 1703–1712.

0022-3263/94/1959-3040$04.50/0

Scheme 2

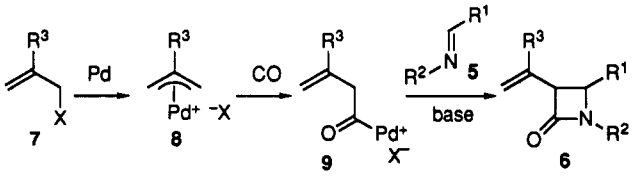


Table 1. Carbonylation of Several Allylic Substrates[a]

entry	temp, °C	7: X	results
1	50	**7a**: Br	only **5a** was detected
2[b]	50	**7b**: OAc	no **6a** was detected
3	50	**7c**: OPh	no reaction
4	50	**7d**: OCO_2Me	no **6a** was detected
5	70	**7e**: SO_2Ph	no reaction
6	50	**7f**: $OP(O)(OEt)_2$	**6a** (67%)[c]
7	rt	**7f**: $OP(O)(OEt)_2$	**6a** (42%)[c]
8	70	**7f**: $OP(O)(OEt)_2$	**6a** (72%)[c]
9	70	**7g**: $OP(O)(OPh)_2$	**6a** (48%)[d]
10	70	**7h**: $OP(O)(Oallyl)_2$	**6a** (33%)[c]

[a] **7** (0.75 mmol), **5a** (0.5 mmol), $Pd_2dba_3CHCl_3$ (2 mol % based on **7**), PPh_3 (8 mol %), i-Pr_2NEt (1.3 equiv), CO (30 kg cm^{-2}), 5 h, THF (5 mL). Yields are isolated yields based on **5a**. [b] NaBr (20 mol %) was added.[7] [c] Only *trans*-**6a** was isolated. [d] ^1H NMR shows a mixture of trans/cis isomers (4.3/1).

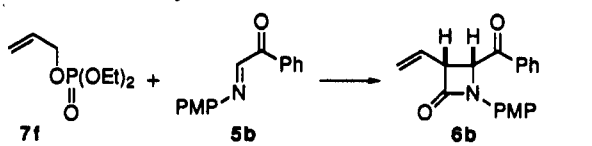
the usefulness and versatility of the method. The generation of a ketene or its equivalent by the carbonylation of an allylic alcohol derivative would provide a new, convenient, and complementary route to β-lactams without the use of a carboxylic acid, its activated form, and activating reagents.

We wish to describe the carbonylation of allylic compound **7** in the presence of imine **5** leading to β-lactam **6** as depicted in Scheme 2.[11] Acyl complex **9** arising from π-allylpalladium **8** by CO insertion has highly acidic protons α to carbonyl. A weak base would abstract the proton to generate a reactive species such as a ketene[12] or a carbanion, which then would add to imine **5** to construct four-membered ring **6**.

Results and Discussion

We first carried out the carbonylation on some allylic derivatives documented to form π-allylpalladium intermediates in the presence of a simple imine such as **5a** (Table 1). It is interesting to note that only phosphates **7f–h** underwent the envisioned cycloaddition to produce desired β-lactam **6a** (entries 6–10), and the stereochemical configuration was trans regardless of the temperature (entries 6-8). These results are contrary to the results reported for the usual ketene–imine cycloaddition[13] in which the reaction of the imines derived from aliphatic amines afforded *cis*-β-lactams and stereoselectivity was

Table 2. Carbonylation in the Presence of Imine 5b[a]



entry	CO, kg cm^{-2}	temp, °C	yield, %[b] **5b**	yield, %[b] **6b**
1	30	50	29	52
2	30	90	14	50
3	30	rt	14	54
4	10	rt	21	31

[a] **7f** (0.45 mmol), **5b** (0.3 mmol), $Pd_2dba_3CHCl_3$ (2 mol % based on **7f**), PPh_3 (8 mol %), i-Pr_2NEt (2 equiv to **5b**), 5 h, THF (5 mL). [b] Isolated yields based on **5b**.

temperature-dependent. The carbonylation of allylic substrates such as bromide **7a**,[14] acetate **7b**,[7] phenyl ether **7c**,[15] carbonate **7d**,[6] and sulfone **7e**[16] gave **6a** in a very low yield, if at all (entries 1–5). The cycloadditions of these allylic compounds, especially acetates and halides,[12] might be realized under more drastic conditions. To obtain a high yield a reaction temperature of 70 °C was required (entry 8), though the reaction proceeds at room temperature (entry 7). Entry 10 shows that only one allyl group of triallyl phosphate participates in the carbonylation.

The preliminary results obtained with allyl phosphate **7f** impelled us to examine another imine for the synthesis of the desired β-lactam. The carbonylative cycloaddition with imine **5b**[17] derived from phenylglyoxal and anisidine was attempted. The results of the investigation of the effects of temperature and pressure are collected in Table 2. The carbonylation requires 30 kg cm^{-2} of CO for efficient cycloaddition (entries 3 and 4), and the reaction with **5b** can be conducted at room temperature, in contrast to that of simple imine **5a** (entries 1–3). Regardless of the reaction temperature, the stereochemistry of product **6b** was always only *cis*, which is remarkably different from the reported selectivity.[13b-d]

The effects of base and solvent on the reaction of phosphate **7f** and imine **5b** are shown in Table 3. Heterogeneous bases were unacceptable (entries 1 and 2). That an amine base was found to be crucial to the success of the reaction indicates that both the steric bulkiness and the basicity of the amine are very important. Use of a stronger base such as DBU and DBN gave no β-lactam (entries 3 and 4), but the addition of a weaker base like collidine produced desired material **6b** in a low yield (entry 7). Neither very hindered amines nor smaller amines were appropriate choices for the purpose (entries 5 and 6). These results imposed the use of c-Hex_2NMe or i-Pr_2NEt for the cycloaddition to attain good yields and exclusive stereoselectivity. Similar requirements have been reported for the carbonylation of phosphates.[7] Solvent also exhibited a marked effect; THF was required for high efficacy (entries 10–14).

(11) For a preliminary report, see; Torii, S.; Okumoto, H.; Sadakane, M.; Hai, A. K. M. A.; Tanaka, H. *Tetrahedron Lett.* **1993**, *34*, 6553–6556.

(12) Guangzhong, W.; Shimoyama, I.; Negishi, E. *J. Org. Chem.* **1991**, *56*, 6506–6507.

(13) For a [2 + 2] cycloaddition of an alkenylketene and an imine, see; (a) Bose, A. K.; Manhas, M. S.; Ghosh, M.; Shah, M.; Raju, V. S.; Bari, S. S.; Newaz, S. N.; Banik, B. K.; Chaudhary, A. G.; Barakat, K. J. *J. Org. Chem.* **1991**, *56*, 6968–6970. (b) Manhas, M. S.; Ghosh, M.; Bose, A. K. *J. Org. Chem.* **1990**, *55*, 575–580. (c) Bose, A. K.; Krishnan, L.; Wagle, D. R.; Manhas, M. S. *Tetrahedron Lett.* **1986**, *27*, 5955–5958. (d) Zamboni, R.; Just, G. *Can. J. Chem.* **1979**, *57*, 1945–1948. (e) Bose, A. K.; Spiegelman, G.; Manhas, M. S. *Tetrahedron Lett.* **1971**, 3167–3171.

(14) (a) Tsuji, J.; Kiji, J.; Imamura, S.; Morikawa, M. *J. Am. Chem. Soc.* **1964**, *86*, 4350–4353. (b) Dent, W. T.; Long, R.; Whitfield, G. H. *J. Chem. Soc.* **1964**, 1588–1594. (c) Merrifield, J. H.; Godschalx, J. P.; Stille, J. K. *Organometallics* **1984**, *3*, 1108–1112.

(15) Tsuji, J.; Kobayashi, Y.; Kataoka, H.; Takahashi, T. *Tetrahedron Lett.* **1980**, *21*, 1475–1478.

(16) Trost, B. M.; Schmuff, N. R.; Miller, M. J. *J. Am. Chem. Soc.* **1980**, *102*, 5979–5981.

(17) Lynch, J. E.; Riseman, S. M.; Laswell, W. L.; Tschaen, D. M.; Volante, R. P.; Smith, G. B.; Shinkai, I. *J. Org. Chem.* **1989**, *54*, 3792–3796. Tschaen, D. M.; Fuentes, L. M.; Lynch, J. E.; Laswell, W. L.; Volante, R. P.; Shinkai, I. *Tetrahedron Lett.* **1988**, *29*, 2779–2782.

Table 3. Cycloaddition of 7f and 5b[a]

entry	base	solvent	yield of 6b, %[b]
1	K_2CO_3	THF	0
2	AcONa	THF	0
3	DBU	THF	0
4	DBN	THF	0
5	Ph_3N	THF	0
6	Et_3N	THF	0
7	2,4,6-collidine	THF	29
8	n-Bu_3N	THF	44
9	i-Pr_2NEt	THF	54
10	c-Hex_2NMe	THF	58
11	c-Hex_2NMe	benzene	38
12	c-Hex_2NMe	CH_2Cl_2	0
13	c-Hex_2NMe	MeCN	0
14	c-Hex_2NMe	DMF	trace

[a] Base (2 equiv to 5b), solvent (5 mL), CO (30 kg cm^{-2}), rt, 5 h. [b] Isolated yield.

Table 4. Cycloaddition of 7f and 5b with Various Catalysts[a]

entry	catalyst/ligand	yield of 6b, %[b]
1	$Pd_2dba_3CHCl_3$/non	0[c]
2	$Pd_2dba_3CHCl_3$/4PPh_3	58
3	$Pd_2dba_3CHCl_3$/6PPh_3	47
4	$Pd_2dba_3CHCl_3$/8PPh_3	46
5	$Pd_2dba_3CHCl_3$/P(*p*-MeOPh)$_3$ (1/4)	36
6	$Pd_2dba_3CHCl_3$/P(*o*-tol)$_3$ (1/4)	31
7	$Pd_2dba_3CHCl_3$/dppe (1/2)	20
8	$Pd_2dba_3CHCl_3$/P(OPh)$_3$ (1/4)	0
9	$Pd(OAc)_2$/2PPh_3	49
10	$PdCl_2(PPh_3)_2$	0[d]

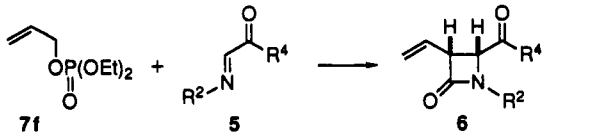
[a] Carried out at rt under CO (30 kg cm^{-2}) in the presence of c-Hex_2NMe. [b] Isolated yield. [c] 7f (90%) and 5b (83%) were recovered. [d] 7f (78%) and 5b (70%) were recovered.

If the ketene were actually liberated, the active species would form a complex with the Pd catalyst,[4] and the ligands would be expected to play an important role in controlling both the stereochemistry and the reactivity. A series of the Pd catalysts with various ligands were explored, and some representative results are summarized in Table 4. The use of $Pd_2dba_3CHCl_3$ complex in combination with PPh_3 was most favored (entry 2). Two equivalents of the ligand per Pd atom were sufficient; larger excesses of the ligand retarded the process (entries 2–4). The use of other phosphines, such as an electron-rich phosphine [P(*p*-MeOPh)$_3$], a bulky ligand [P(*o*-tol)$_3$], and a bidentate compound (dppe), decreased the yield, but the stereochemistry of product **6b** was only cis in each reaction (entries 5–7). The results shown in entries 1 and 8 indicated that a phosphine ligand is indispensable. Another practical and convenient couple, $Pd(OAc)_2$ and PPh_3, also effectively catalyzed the carbonylation (entry 9).

With these optimized reaction conditions, the carbonylation was extended to various other imines **5**. Table 5 presents the results of the reactions with imines **5c–5e**, which are conjugated with a carbonyl. Lactams **6c** and **6d** were prepared from keto imines **5c** and **5d**, respectively, at room temperature in good yields (entries 1 and 2). The carbonylations with imines **5c-e**, derived from both aliphatic and aromatic amines, afforded *cis*-β-lactams **6c-e** with high stereoselectivity in spite of their susceptibility to epimerization.[17] Contrary to what has been reported in the literature,[13b–d] the nature of the amine moiety is not responsible for the stereocontrol of the cycloaddition.

In sharp contrast to the above results, the cycloadditions employing imines **5**, that are not conjugated with a carbonyl, resulted in the predominant formation of *trans*-

Table 5. Cycloaddition Using Imines Conjugated with Carbonyl[a]

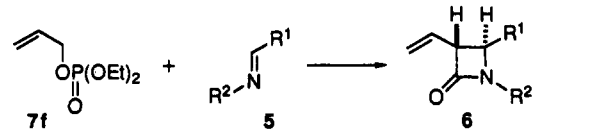


7f 5 6

entry	imine 5 R²	imine 5 R⁴	yield of 6 (%)
1	5c: Pr	Ph	6c (50)[b]
2	5d: $CH_2CH(OMe)_2$	Ph	6d (63)[c]
3	5e: PMP	OMe	6e (11)[d]

[a] Carried out at rt under CO (30 kg cm^{-2}) in the presence of c-Hex_2NMe. [b] Only *cis*-6c was isolated. [c] ^1H NMR shows a mixture of cis/trans isomers (5/1). [d] Carried out at 70 °C to give a mixture of cis/trans isomers (6/1).

Table 6. Reaction with Imines Nonconjugated with Carbonyl[a]



7f 5 6

entry	imine 5	R¹	R²	6 (%)[b]
1	5f:	Ph	Bn	6f (73)
2[c]	5f:	Ph	Bn	6f (27)
3	5g:	Ph	PMB	6g (70)
4	5h:	Ph	PMP	6h (0)
5	5i:	2-furyl	Bn	6i (86)
6	5j:[d]	2-furyl	CH_2COOBn	6j (47)
7	5k:[d]	–C(Me)=CHPh	Bn	6k (47)[e]
8	5l:	–C(Me)=CHPh	CH_2COOBn	6l (61)[e]
9	5m:	–C(Me)=CHPh	PMP	6m (<4)[f]
10	5n:	OMe	Bn	6n (0)

[a] Carried out at 70 °C under CO (30 kg cm^{-2}) in the presence of i-Pr_2NEt to give *trans*-6, unless otherwise stated. [b] Isolated yield. [c] Carried out at rt. [d] The imine was not pure due to the instability. [e] ^1H NMR shows a mixture of trans/cis isomers (4/1–8/1). [f] Detected by ^1H NMR.

β-lactams **6**. As can be seen in Table 6, the reaction proceeded smoothly at 70 °C but was sluggish at room temperature. The carbonylative cycloadditions with stable imines **5f**, **5g**, and **5i** led to the corresponding β-lactams **6** in high yields (entries 1, 3, and 5), whereas β-lactams **6j** and **6k** were obtained in lower yields because of the instability of imines **5j** and **5k** (entries 6 and 7). The corresponding cis isomers were not detected by ^1H NMR analysis (200 MHz) in most of the cases, even though the reaction was carried out at room temperature (entry 2). Some contamination by the cis isomers was observed in the reactions of imines **5k** and **5l**, which are homologated with olefin, as indicated in Entries 7 and 8. That electron-rich imines such as **5h**, **5m**, and **5n** did not react (entries 4, 9, and 10) is valuable evidence for the reaction mechanism.

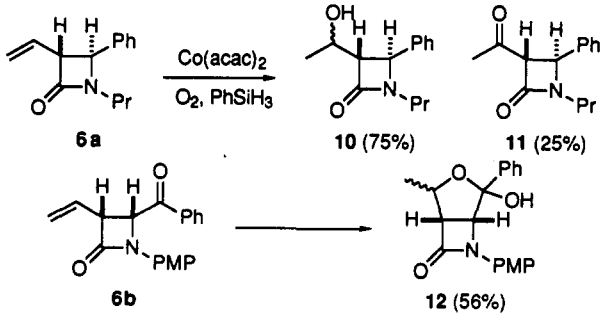
The dependency of the stereochemical outcome on the nature of the imine employed has often been observed.[5,17] The precedents from cycloadditions of alkenylketene and imine indicate that the *cis*-lactams are produced from imines derived from aliphatic amines, and the trans compounds stem from imines derived from arylamines under affection of the temperature for the selectivity, although no unambiguous generalizations on the steric course have been made.[13] However, it is not the amine fragment but the aldehyde fragment of the imine that

Table 7. Cycloaddition Using Substituted Phosphates

entry	phosphate 7[a]	imine 5	yield of 6 (%)
1	7i: R^3 = Me	5i	6p (98)[b]
2	7i: R^3 = Me	5b	6q (38)[c]
3	7j: R^3 = $CH_2OTBDMS$	5i	6r (64)[b]
4	7j: R^3 = $CH_2OTBDMS$	5b	6s (36)[c]

[a] Phosphates [X=OP(O)(OEt)$_2$] were used. [b] Carried out at 70 °C using i-Pr_2NEt. Only *trans*-lactam was obtained. [c] Carried out at rt using c-Hex_2NMe to give only *cis*-lactam.

Scheme 3



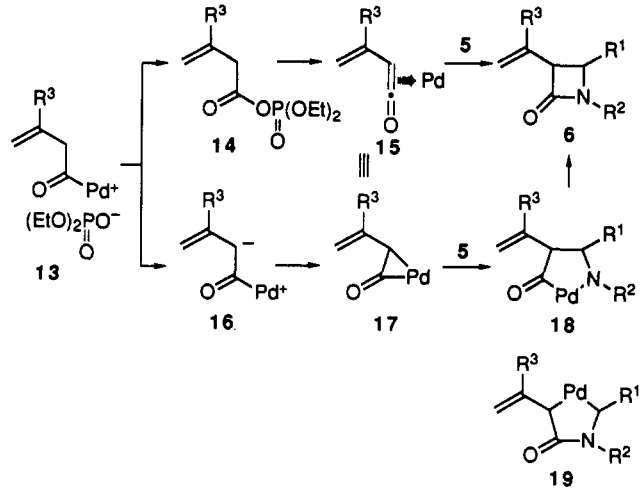
provides the stereocontrol in the carbonylative cycloaddition. The imines derived from vicinal dicarbonyl substances afford *cis*-lactams (Tables 2–5), whereas the imines prepared from aryl and alkenyl aldehydes afford *trans*-lactams (Tables 1 and 6). The different basis for the stereoselection in this carbonylative cycloaddition is worthy of emphasis.

After the assessment of the imine partner, substituted allylic phosphates were investigated. The carbonylations of phosphates **7i** and **7j** were performed as represented in Table 7. Methacryl phosphate **7i** underwent the carbonylative cycloaddition with imine **5i** very efficiently to give rise to the corresponding *trans*-lactam **6p** quantitatively (entry 1). Functionalized phosphate **7j** also served as an effective precursor for the purpose (entries 3 and 4). It should be noted that again the reactions exclusively gave one or the other stereoisomer. The reaction with keto-imine **5b** gave *cis*-lactams **6q** and **6s**, whereas imine **5i** was transformed into trans compounds **6p** and **6r**. None of the other stereoisomers was isolated in either attempt. Thus, the usefulness of the carbonylative cycloaddition has been exemplified by the synthesis of a series of β-lactams **6** bearing useful substituents at positions relevant for further structural modifications.

The usefulness of the carbonylative cycloaddition requires further elaboration of the products. The lack of a convenient method for the conversion of the vinyl group at the 3 position into an appropriate appendage, particularly a hydroxyethyl group, may relegate the cycloaddition of vinylketene into a comparatively less attractive approach to the synthesis of carbapenam congeners.[13b,c] The Co-catalyzed oxygenation recently reported by Mukaiyama et al. met our purpose.[18] Treatment of lactam **6a** with phenylsilane in the presence of Co(acac)$_2$ under an O_2 atmosphere smoothly afforded anticipated alcohol **10** in a satisfactory yield together with ketone **11** (Scheme 3), although the stereochemistry of the hydroxy group was unfortunately not controlled. The same procedure for keto lactam **6b** resulted in the formation of hemiacetal **12**, which will be a useful intermediate for the synthesis of carbapenams.[17]

(18) Isayama, S.; Mukaiyama, T. *Chem. Lett.* **1989**, 1071–1074.

Scheme 4

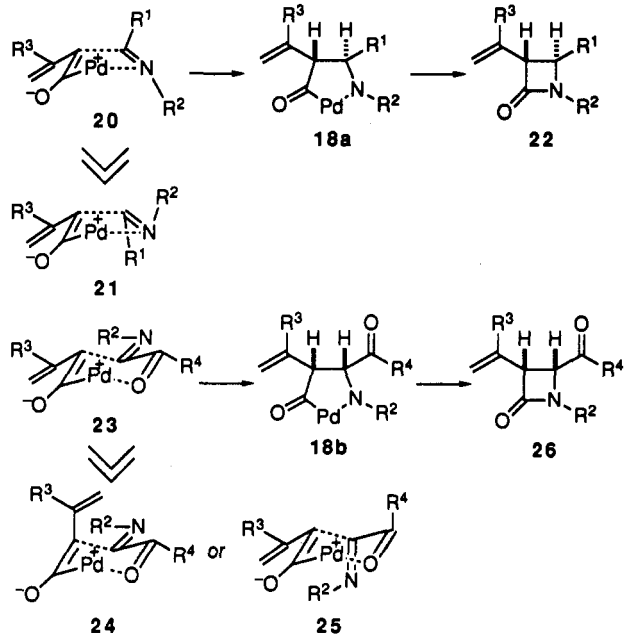


The mechanism of this carbonylative formal [2 + 2] cycloaddition delineated above deserves discussion. Though further investigations are necessary to explain the actual sequence of events, some of the results already available allow us to propose the reaction paths depicted in Schemes 4 and 5. Direct generation of ketene **15**, which is probably complexed with Pd, by means of the elimination of HPdX from acylpalladium **13** is one possibility, since the liberation of ketene is presumed in a Pd-catalyzed carbonylation.[12] However, such a β-elimination from an acylmetal species is not generally observed, although an example has been reported for a Ru complex.[4h] Another way to ketene **15** via acyl phosphate **14**, possibly produced in a manner similar to the preparation of acid chlorides by Pd-catalyzed carbonylation of allyl chlorides,[14a] is conceivable. The results from an analogous intermediate[10] indicate that acyl phosphate **14** should serve as an activated acyl derivative. However, carbonylations in the presence of several olefins and electron-rich acetylenes[5b,19] to corroborate the vinylketene formation failed to afford the corresponding cycloadducts. The above-mentioned reaction paths do not sufficiently account for the encountered differences between this carbonylation and the usual ketene–imine cycloadditions. The stereocontrol of β-lactam generation was revealed to be based on a different reason than that of the reactions[13] of acid chlorides with triethylamine. Although ketene formation can not be excluded, we can consider other routes involving the abstraction of the α-proton of **13**. An intramolecular substitution reaction between the Pd center and the carbanion in **16** would be expected to release three-membered intermediate **17**,[20] which is, except for the vinyl group, almost the same as known late transition metal–ketene complexes.[4j,l] Insertion of imine **5** into metallacycle **17** would produce lactam **6** by way of **18** or **19**. However, the deprotonation of the acylpalladium complex has been reported to give an enolate rather than either a ketene or a three-membered intermediate like **17**,[4d] and the Pd-catalyzed carbonylation yielding cyclobutanone[12] did not

(19) Danheiser, R. L.; Gee, S. K.; Perez, J. J. *J. Am. Chem. Soc.* **1986**, *108*, 806-810. Jackson, D. A.; Rey, M.; Dreiding, A. S. *Tetrahedron Lett.* **1983**, *24*, 4817–4820, and refs therein.

(20) Formation of C,O-η^2-ketene complexes by deprotonation of acylmetals has been reported for early transition metals, see; Ho, S. C. H.; Straus, D. A.; Armantrout, J.; Schaefer, W. P.; Grubbs, R. H. *J. Am. Chem. Soc.* **1984**, *106*, 2210–2211. Moore, E. J.; Straus, D. A.; Armantrout, J.; Santarsiero, B. D.; Grubbs, R. H.; Bercaw, J. E. *J. Am. Chem. Soc.* **1983**, *105*, 2068–2070. Straus, D. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **1982**, *104*, 5499–5500, and refs cited therein.

Scheme 5



accompany cyclopropane adducts that were observed in the reaction of a Pt–ketene complex.[4j] In addition, these mechanisms fail to account for the unique stereocontrol. Thus, the actually reactive species may be neither free vinylketene nor three-membered ketene–Pd complex. It still remains unclear why the highly selective distribution of the *cis*- and *trans*-lactams depends on the nature of the original aldehyde component of the imine and why electron-rich imines such as **5h**, **5m**, and **5n** do not react, as they do in the ordinary cycloaddition.[13b-d]

Reconsideration of the reaction course involving carbanion **16** and metallacycle **18** led us to propose an alternative path. Taking into account the high dependency of the reaction upon the nature of the imine and the report[4d] postulating the formation of an enol from an acylpalladium, we can regard the C–C bond-forming process as a nucleophilic addition of enolate **16** to imine **5**.[21] As illustrated in Scheme 5,[22] the sequence is principally governed by the steric effects.[5a] When the imine contains no carbonyl, coordination of the nitrogen atom to the Pd atom leads to a five-membered transition state. The process would favor intermediate **20**, which is less congested than **21**, to give rise to *trans*-lactam **22** through metallacycle **18a**. In fact, the reactions shown in Table 6 gave *trans*-lactams at 70 °C. The failure of electron-rich imines such as **5h**, **5m**, and **5n** to react to an appreciable extent can be ascribed to their relatively lower electrophilicity. Conjugation with a carbonyl group enhances the electrophilicity of the imine, and the carbonyl can chelate to the Pd atom to form six-membered cyclic transition states **23–25**. Hence, the nucleophilic addition is significantly facilitated, and the steric circumstances direct the reaction to proceed through the most-stable transition state **23**, which affords *cis*-lactam **26**, via cis adduct **18b**, in preference to the path through **24** or **25**. The experimental results are in good agreement with this mechanism. For instance, the cycloadditions with the imines in Tables 2, 5, and 7 were realized at room temperature because of the comparatively high electrophilicity of the imines and gave cis products. Thus, both the unique stereocontrol and the characteristic reactivity of the imines support the nucleophilic addition process affording a formal [2 + 2] cycloadduct.[23]

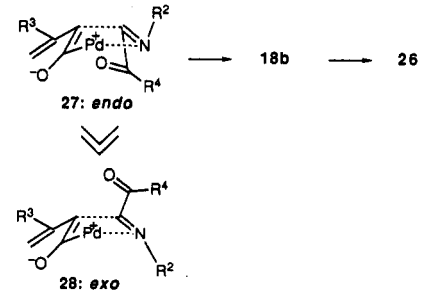
Conclusion

Intramolecular transition metal assisted carbonylations constitute an important method for the construction of the β-lactam structure.[24] Hegedus described β-lactam synthesis using ketenes photolytically generated from stoichiometric carbene complexes.[25] The [2 + 2] cycloaddition of alkenylketenes and imines has proved useful.[5,13] The catalytic carbonylation of allyl phosphate **7**, a new ketene equivalent, provides a convenient route to the β-lactam framework with unique stereocontrol. The construction of a wide range of 3-alkenyl β-lactams with a stereodefined array of appropriate substituents should be feasible through the appropriate choice of the reaction partners.

(21) Enolates of iron acyls have been utilized as nucleophiles, see; Ojima, I.; Kwon, H. B. *J. Am. Chem. Soc.* **1988**, *110*, 5617–5621. Liebeskind, L. S.; Welker, M. E.; Fengl, R. W. *J. Am. Chem. Soc.* **1986**, *108*, 6328–6343. Davies, S. G.; Walker, J. C. *J. Chem. Soc., Chem. Commun.* **1985**, 209–210, and refs cited therein.

(22) A number of β-lactam syntheses by nucleophilic addition of enolates to imines have been developed.[5a] However, these reactions can not form cyclic transition states such as those illustrated in Scheme 5 because the chelating metals of the enolates are not on the acyl carbon but on the oxygen. For a recent example of an enolate approach and a determination of the (*E*)-geometry of the imine, see; Hattori, K.; Miyata, M.; Yamamoto, H. *J. Am. Chem. Soc.* **1993**, *115*, 1151–1152.

(23) Negishi's results[12] in conjunction with our experiments suggest the participation of the other reactive species. The reaction pathway through 1,3-dipolar cycloaddition depicted below seems to be more attractive. However, to our knowledge, no 1,3-dipoles consisting of a metal terminus are known. Zwitterion **16**, which involves an anion and a cation proximate to a π-bond, may be capable of acting as a 1,3-dipole. In the case of the imines that are not conjugated with carbonyl, intermediate **20** in the nucleophilic route (Scheme 5) can also be considered as the transition state of the [π4s + π2s] concerted process, wherein the stereocontrol is due to the steric interaction. The homologation of the π-system with an olefin in imines **5k** and **5l** calls for some contribution of the stereoelectronic effect resulting in a decrease of the selectivity. On the other hand, the keto imines possessing lower LUMO levels undergo cycloaddition more readily under stereoelectronic control. The secondary orbital interaction caused by such conjugation makes *endo*-transition state **27** preferred over *exo*-mode **28**, giving rise to *cis*-lactam **26**. Thus, the formal [2 + 2] cycloaddition proceeds through initial 1,3-dipolar cycloaddition followed by reductive elimination or reductive displacement. The sequence can reasonably account for both our reactions and Negishi's. For reviews of 1,3-dipolar cycloadditions, see; Carruthers, W. *Cycloaddition Reactions in Organic Synthesis;* Pergamon Press: Oxford, 1990, pp 269–331. Padwa, A.; Schoffstall, A. M. In *Advances in Cycloaddition;* Curran, D. P., Ed.; JAI Press Inc.: Greenwich, 1990; Vol. 2, pp 1–89.



(24) Torii, S.; Okumoto, H.; Sadakane, M.; Xu, L. H. *Chem. Lett.* **1991**, 1673–1676. Mandai, T.; Ryoden, K.; Kawada, M.; Tsuji, J. *Tetrahedron Lett.* **1991**, *32*, 7683–7686. Matsuda, I.; Sakakibara, J.; Nagashima, H. *Tetrahedron Lett.* **1991**, *32*, 7431–7434. Spears, G. W.; Nakanishi, K.; Ohfune, Y. *Synlett* **1991**, 91–92. Calet, S.; Urso, F.; Alper, H. *J. Am. Chem. Soc.* **1989**, *111*, 931–934. Alper, H.; Hamel, N. *Tetrahedron Lett.* **1987**, *28*, 3237–3240. Mori, M.; Chiba, K.; Okita, M.; Kayo, I.; Ban, Y. *Tetrahedron* **1985**, *41*, 375–385. Hodgson, S. T.; Hollinshead, D. M.; Ley, S. V. *Tetrahedron* **1985**, *41*, 5871–5878. Aida, T.; Legault, R.; Dugat, D.; Durst, T. *Tetrahedron Lett.* **1979**, 4993–4994. Wong, P. K.; Madhavarao, M.; Marten, D. F.; Rosenblum, M. *J. Am. Chem. Soc.* **1977**, *99*, 2823–2824.

(25) Narukawa, Y.; Juneau, K. N.; Snustad, D.; Miller, D. B.; Hegedus, L. S. *J. Org. Chem.* **1992**, *57*, 5453–5462, and refs cited therein.

Experimental Section

General. THF was distilled from Na/benzophenone under Ar. $Pd_2dba_3CHCl_3$ was used as obtained from Aldrich Chemical Co., and PPh_3 was used after recrystallization from hexane. NMR spectra were measured with $CDCl_3$ as a solvent and an internal standard at 200 MHz and/or 500 MHz for ^1H NMR and at 50 MHz for ^{13}C NMR. Chemical shifts are expressed in ppm and the J values are in hertz. The imines were prepared from the corresponding aldehydes and amines by the literature methods[13,17] and were used without purification. The phosphates were obtained according to the literature method.[26] The carbonylations summarized in the tables were carried out according to the following general procedures unless otherwise specified in the tables and their footnotes. The isolated yields in the tables were calculated based on the amount of imine employed. The ratios of the cis/trans isomers were determined by ^1H NMR analysis.

A General Procedure for the Carbonylative Cycloaddition. Into a 20-mL thick glass tube was added a solution of imine **5** (0.5 mmol) and allyl phosphate **7** (0.75 mmol) in THF (5 mL). Then c-Hex_2NMe (1.0 mmol), $Pd_2dba_3CHCl_3$ (2 mol %), and Ph_3P (8 mol %) were added. The glass tube was placed in a stainless steel autoclave, which was then charged with CO gas at 30 kg cm^{-2}. After being stirred for 5 h at rt, the reaction mixture was poured into water and extracted with EtOAc three times. The combined extracts were washed with brine and dried (Na_2SO_4). Filtration followed by concentration afforded a viscous mass, which was purified by SiO_2 column chromatography using toluene–EtOAc as an eluent to give β-lactam **6**. The carbonylation of keto imines **5b**, **5c**, **5d**, and **5e** gave the corresponding cis-β-lactams **6b**, **6c**, **6d**, **6e**, **6q**, and **6s**. The yields are summarized in the tables and the physical data are collected as follows.

***cis*-1-(4-Methoxyphenyl)-3-vinyl-4-benzoyl-2-azetidinone (6b):**[13c] IR (neat) 1640 (C=C), 1688 (C=O), 1748 (C=O) cm^{-1}; ^1H NMR δ 3.75 (s, 3), 4.40 (dd, 1, J = 8.8, 6.3), 5.14 (dd, 1, J =10.3, 1.4), 5.37 (dd, 1, J = 17.1, 1.4), 5.54 (ddd, 1, J = 17.1, 10.3, 8.8), 5.61 (d, 1, J = 6.3), 6.82–7.93 (m, 9); ^{13}C NMR δ 55.41, 57.33, 59.57, 114.25, 118.41, 122.79, 127.37, 128.21, 128.94, 130.99, 134.15, 134.86, 156.30, 162.85, 193.33; MS m/z 307 (M^+). Anal. Calcd for $C_{19}H_{17}NO_3$: C, 74.25; H, 5.58; N, 4.56. Found: C, 74.26; H, 5.64; N, 4.40.

***cis*-1-Propyl-3-vinyl-4-benzoyl-2-azetidinone (6c):** IR (neat) 1635 (C=C), 1690 (C=O), 1748 (C=O) cm^{-1}; ^1H NMR δ 0.91 (t, 3, J = 7.8), 1.53 (m, 2), 3.2 (m, 1), 3.5 (m, 1), 4.25 (dd, 1, J = 5.9, 8.3), 5.05 (m, 1), 5.2 (d, 1, J = 5.9), 5.26 (m, 1), 5.44 (ddd, 1, J = 8.3, 9.77, 16.99), 7.5 (m, 3), 7.85 (m, 2); ^{13}C NMR δ 11.50, 20.76, 43.36, 58.01, 59.55, 122.04, 127.93, 128.00, 128.80, 133.93, 134.84, 166.15, 195.08; MS m/z 243 (M^+); HRMS calcd for $C_{15}H_{17}NO_2$ 243.1259, found 243.1226.

***cis*-1-(2,2-Dimethoxyethyl)-3-vinyl-4-benzoyl-2-azetidinone (6d).** By means of the general procedure, the carbonylation of imine **5d** gave a mixture (5/1) of compound **6d** and its trans isomer: IR (neat) 1640 (C=C), 1690 (C=O), 1748 (C=O) cm^{-1}; ^1H NMR δ 3.28 (s, 3), 3.29 (s, trans isomer), 3.33 (s, 3), 3.34 (s, trans isomer), 3.4 (dd, 1, J = 5.64, 14.55), 3.67 (dd, J = 2.74, 9.06, trans isomer), 3.78 (dd, 1, J = 4.35, 14.55), 4.28 (dd, 1, J = 5.91, 8,4), 4.48 (dd, 1, J = 4.35, 5.64), 4.94 (d, J = 2.74, trans isomer), 5.08 (dd, 1, J = 1.74, 9.80), 5.26 (dd, 1, J = 1.74, 17.0), 5.35 (d, 1, J = 5.91), 5.45 (ddd, 1, J = 8.4, 9.80, 17.0), 7.5 (m, 3), 7.85 (m, 2); ^{13}C NMR δ 12.14, 53.76, 53.89, 58.51, 60.58, 101.89, 121.95, 127.78, 127.95, 128.75, 133.81, 135.04, 166.42, 195.23; MS m/z 289 (M^+).

***cis*-1-(4-Methoxyphenyl)-3-vinyl-4-(methoxycarbonyl)-2-azetidinone (6e).**[13b] By means of the general procedure, the carbonylation of imine **5e** at 70 °C gave a mixture (4/1) of compound **6e** and its trans isomer: IR (neat) 1640 (C=C), 1725 (C=O), 1752 (C=O) cm^{-1}; ^1H NMR δ 3.75 (s, 3), 3.77 (s, 3), 4.3 (m, 1), 4.32 (d, J = 2.49, trans isomer), 4.7 (d, 1, J = 6.24), 5.4 (m, 1), 5.53 (m, 1), 5.75 (m, 1), 6.85 (d, 2, J = 8.95), 7.25 (d, 2, J = 8.95); ^{13}C NMR δ 52.42, 55.44, 56.25, 56.32, 114.36, 117.87, 117.98, 122.79, 127.14, 156.45, 163.17, 168.75.

***cis*-1-(4-Methoxyphenyl)-3-(2-propenyl)-4-benzoyl-2-azetidinone (6q):** IR (KBr) 1645 (C=C), 1688 (C=O), 1740 (C=O) cm^{-1}; ^1H NMR δ 1.49 (s, 3), 3.75 (s, 3), 4.4 (d, 1, J = 6.40), 4.95 (m, 2), 5.63 (d, 1, J = 6.40), 6.82 (d, 2, J = 8.97), 7.28 (d, 2, J = 8.97), 7.55 (m, 3), 7.95 (m, 2); ^{13}C NMR δ 21.41, 55.41, 60.04, 60.89, 114.22, 118.39, 119.11, 128.33, 128.81, 131.04, 134.11, 134.94, 135.65, 156.27, 163.33, 193.21; MS m/z 321 (M^+). Anal. Calcd for $C_{20}H_{19}NO_3$: C, 74.75; H, 5.96; N, 4.36. Found: C, 74.76; H, 5.95; N, 4.35.

***cis*-1-(4-Methoxyphenyl)-3-[1-(*tert*-butyldimethylsiloxy)-propen-2-yl]-4-benzoyl-2-azetidinone (6s):** IR (neat) 1655 (C=C), 1690 (C=O), 1754 (C=O) cm^{-1}; ^1H NMR δ −0.11(s, 6), 0.82 (s, 9), 3.76 (s, 3), 3.65–3.8 (m, 2), 4.55 (d, 1, J = 6.38), 5.16 (s, 1), 5.25 (s, 1), 5.65 (d, 1, J = 6.38), 6.85 (d, 2, J = 8.98), 7.25 (d, 2, J = 8.98), 7.5 (m, 3), 7.95 (m, 2); ^{13}C NMR δ −5.67, −5.56, 18.17, 25.76, 55.44, 55.85, 59.96, 64.59, 114.29, 114.61, 116.52, 118.35, 123.49, 128.26, 128.89, 130.56, 131.06, 133.32, 134.13, 135.17, 138.54, 154.10, 156.31, 163.35, 193.06; MS m/z 451 (M^+). Anal. Calcd for $C_{28}H_{33}NO_4Si$: C, 69.15; H, 7.36; N, 3.10. Found: C, 69.07; H, 7.27; N, 3.11.

The carbonylative cycloadditions with imines that were not conjugated with carbonyl groups were carried out under slightly modified conditions using i-Pr_2NEt in place of c-Hex_2NMe at 70 °C to give *trans*-β-lactams. The yields are collected in the tables, and the physical data are as follows.

***trans*-1-Propyl-3-vinyl-4-phenyl-2-azetidinone (6a):** IR (neat) 1638 (C=C), 1756 (C=O) cm^{-1}; ^1H NMR δ 0.89 (t, 3, J = 7.44), 1.5 (m, 2), 2.8 (m, 1), 3.44 (m, 1), 3.6 (brd, 1, J = 7.80), 4.33 (d, 1, J = 2.12), 5.26 (m, 2), 5.99 (ddd, 1, J = 17.4, 10.25, 7.80), 7.35 (m, 5); ^{13}C NMR δ 11.37, 20.92, 42.18, 61.32, 63.79, 119.03, 126.30, 128.50, 128.94, 131.22, 137.54, 168.15; MS m/z 215 (M^+).

***trans*-1-Benzyl-3-vinyl-4-phenyl-2-azetidinone (6f):** IR (neat) 1638 (C=C), 1748 (C=O) cm^{-1}; ^1H NMR δ 3.66 (dd, 1, J = 2.23, 7.81), 3.77 (d, 1, J = 14.97), 4.2 (d, 1, J = 2.23), 4.86 (d, 1, J = 14.97), 5.25 (m, 2), 5.9 (ddd, 1, J = 7.81, 10.3, 17.1), 7.25 (m, 10); ^{13}C NMR δ 44.32, 60.51, 63.88, 119.11, 126.34, 127.59, 128.24, 128.45, 128.64, 128.89, 130.78, 135.32, 136.96, 167.87; MS m/z 263 (M^+).

***trans*-1-(4-Methoxybenzyl)-3-vinyl-4-phenyl-2-azetidinone (6g):** IR (neat) 1638 (C=C), 1744 (C=O) cm^{-1}; ^1H NMR δ 3.65 (dd, 1, J = 7.75, 2.17), 3.75 (d, 1, J =14.81), 3.78 (s, 3), 4.18 (d, 1, J = 2.17), 4.8 (d, 1, J = 14.81), 5.25 (m, 2), 5.9 (ddd, 1, J = 7.75, 10.26, 17.15), 6.8–7.4 (m, 9); ^{13}C NMR δ 43.74, 55.07, 60.31, 63.72, 113.97, 118.98, 126.32, 127.36, 128.37, 128.85, 129.56, 130.82, 137.10, 158.98, 167.72; MS m/z 293 (M^+); Anal. Calcd for $C_{19}H_{19}NO_2$: C, 77.79; H, 6.53; N, 4.77. Found: C, 77.53; H, 6.45; N, 4.56.

***trans*-1-Benzyl-3-vinyl-4-(2-furyl)-2-azetidinone (6i):** IR (neat) 1640 (C=C), 1744 (C=O) cm^{-1}; ^1H NMR δ 3.85 (d, 1, J = 15.1), 4.0 (dd, 1, J =2.33, 7.6), 4.26 (d, 1, J = 2.33), 4.7 (d, 1, J = 15.1), 5.27 (m, 2), 5.9 (ddd, 1, J = 7.6, 10.3, 17.15), 6.3 (m, 2), 7.2 (m, 5), 7.38 (brs, 1); ^{13}C NMR δ 44.61, 53.67, 60.06, 109.47, 110.43, 119.28, 127.54, 128.13, 128.60, 130.54, 135.32, 143.11, 149.68, 167.42; MS m/z 253 (M^+); HRMS calcd for $C_{16}H_{15}NO_2$ 253.1103, found 253.1104.

***trans*-1-[(Benzyloxycarbonyl)methyl]-3-vinyl-4-(2-furyl)-2-azetidinone (6j):** IR (neat) 1640 (C=C), 1688 (C=O), 1744 (C=O) cm^{-1}; ^1H NMR δ 3.5 (d, 1, J = 18.12), 4.03 (brd,1, J = 7.86), 4.35 (d, 1, J = 18.12), 4.69 (d, 1, J = 2.5), 5.14 (d, 2, J = 2.22), 5.3 (m, 2), 5.9 (ddd, 1, J = 7.86, 10.2, 17.15), 6.35 (m, 2), 7.4 (m, 6); ^{13}C NMR δ 41.50, 54.83, 60.81, 67.22, 109.66, 110.54, 118.12, 119.74, 128.18, 128.23, 128.35, 128.45, 128.53, 128.58, 130.23, 134.87, 135.15, 143.36, 149.43, 167.79, 167.86; MS m/z 311 (M^+); HRMS calcd for $C_{18}H_{17}NO_4$ 311.1157, found 311.1165. Anal. Calcd for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.04; H, 5.54; N, 4.23.

***trans*-1-Benzyl-3-vinyl-4-(1-phenylpropen-2-yl)-2-azetidinone (6k).** By means of the modified general procedure, the carbonylation in the presence of imine **5k** gave a mixture (4/1) of compound **6k** and its cis isomer: IR (neat) 1638 (C=C), 1744 (C=O) cm^{-1}; ^1H NMR δ 1.72 (s, cis isomer), 1.78 (s, 3), 3.1 (d, J = 6.24, cis isomer), 3.64 (brd, 1, J = 7.82), 3.84 (d, 1, J = 2.1), 4.09 (d, 1, J = 15.0), 4.75 (d, 1, J = 15.0), 5.25 (m, 2), 5.9 (ddd, 1, J = 7.82, 10.37, 17.09), 6.44 (s, 1), 7.28 (m, 10); ^{13}C NMR δ 12.92, 45.11, 59.15, 64.81, 119.08, 126.93, 127.68, 128.17, 128.51, 128.68, 128.83, 129.26, 131.11, 133.44, 135.49, 136.58, 167.67; MS m/z 303 (M^+); HRMS calcd for $C_{21}H_{21}NO$ 303.1623, found 303.1598.

(26) Murahashi, S.; Taniguchi, Y.; Imada, Y.; Tanigawa, Y. *J. Org. Chem.* **1989**, *54*, 3292–3303.

***trans*-1-[(Benzyloxycarbonyl)methyl]-3-vinyl-4-(1-phenylpropen-2-yl)-2-azetidinone (6l).** By means of the modified general procedure, the carbonylation in the presence of imine **5l** gave a mixture (8/1) of compound **6l** and its cis isomer: IR (neat) 1640 (C=C), 1670 (C=O), 1746 (C=O), 1760 (C=O) cm^{-1}; ^1H NMR δ 1.87 (s, 3), 1.88 (s, cis isomer), 3.62 (d, 1, J = 18.07), 3.7 (brd, 1, J = 7.32), 4.22 (d, 1, J = 2.23), 4.45 (d, 1, J = 18.07), 5.19 (s, 2), 5.35 (m, 2), 6.0 (ddd, 1, J = 8.2, 10.2, 17.09), 6.42 (s, cis isomer), 6.5 (s, 1), 7.3 (m, 10); ^{13}C NMR δ 13.21, 41.86, 60.14, 65.42, 67.20, 119.39, 126.94, 128.14, 128.31, 128.36, 128.53, 128.75, 128.82, 130.81, 133.02, 134.83, 136.37, 167.70, 168.20; MS m/z 361 (M^+); HRMS calcd for $C_{23}H_{23}NO_3$ 361.1677, found 361.1697.

***trans*-1-Benzyl-3-(2-propenyl)-4-(2-furyl)-2-azetidinone (6p):** IR (neat) 1649 (C=C), 1744 (C=O) cm^{-1}; ^1H NMR δ 1.79 (s, 3), 3.88 (d, 1, J = 15.05), 4.02 (brd, 1, J = 1.46), 4.33 (d, 1, J = 2.44), 4.78 (d, 1, J = 15.05), 4.95 (m, 2), 6.30 (m, 2), 7.25 (m, 5), 7.38 (brs, 1); ^{13}C NMR δ 20.05, 44.54, 52.48, 63.25, 109.22, 110.42, 114.22, 127.53, 128.18, 128.58, 135.39, 138.01, 143.08, 150.08, 167.33; MS m/z 267 (M^+).

***trans*-1-Benzyl-3-[1-[(*tert*-butyldimethylsiloxy)propen-2-yl]-4-(2-furyl)-2-azetidinone (6r):** IR (neat) 1657 (C=C), 1760 (C=O) cm^{-1}; ^1H NMR δ −0.013 (s, 3), −0.005 (s, 3), 0.84 (s, 9), 3.85 (d, 1, J = 15.10), 4.03 (brs, 1), 4.1 (s, 2), 4.35 (d, 1, J = 2.44), 4.75 (d, 1, J = 15.10), 5.2 (m, 2), 6.28 (m, 2), 7.2 (m, 5), 7.38 (brd, 1, J = 1.95); ^{13}C NMR δ −5.62, −5.56 18.19, 25.74, 44.62, 53.71, 59.24, 64.79, 109.37, 110.41, 112.09, 127.52, 128.14, 128.59, 135.45, 141.85, 143.01, 150.07, 167.24; MS m/z 397 (M^+). Anal. Calcd for $C_{23}H_{31}NO_3Si$: C, 69.48; H, 7.86; N, 3.52. Found: C, 69.21; H, 8.12; N, 3.35.

Co-Catalyzed Oxygenation of Vinyl Group.[18] To a solution of phenylsilane (0.05 mL, 0.40 mmol) and $Co(acac)_2$ (3 mg, 0.01 mmol) in THF (2 mL) was added a solution of lactam **6a** (43 mg, 0.20 mmol) in THF (0.5 mL). The reaction mixture was stirred at rt for 3 h under an O_2 atmosphere. After completion of the reaction, the volatile materials were evaporated under reduced pressure. The crude product was chromatographed on SiO_2 to afford alcohol **10** (35 mg, 75%) together with ketone **11** (11.5 mg, 25%).

***trans*-1-Propyl-3-(1-hydroxyethyl)-4-phenyl-2-azetidinone (10):** IR (neat) 1734 (C=O), 3400 (OH) cm^{-1}; ^1H NMR δ 0.9 (t, 3, J = 7.4), 1.29 (d, 3 × 0.55, J = 6.35), 1.35 (d, 3 × 0.45, J = 6.35), 1.5 (m, 2), 2.82 (m, 1), 3.02 (m, 1), 3.4 (m, 1), 4.17 (m, 0.45), 4.29 (m, 0.55), 4.43 (d, 0.45, J = 2.1), 4.67 (d, 0.55, J = 2.1), 7.35 (m, 5); ^{13}C NMR δ 11.44, 20.92, 21.28, 21.33, 42.15, 56.31, 57.39, 64.62, 66.00, 66.15, 66.93, 126.39, 128.22, 128.42, 128.92, 137.80, 138.27, 168.70, 168.82; MS m/z 233 (M^+); HRMS calcd for $C_{14}H_{19}NO_2$ 233.1416, found 233.1426.

***trans*-1-Propyl-3-acetyl-4-phenyl-2-azetidinone (11):** IR (neat) 1715 (C=O), 1758 (C=O) cm^{-1}; ^1H NMR δ 0.87 (t, 3, J = 7.0), 1.5 (m, 2), 2.3 (s, 3), 2.85 (m, 1), 3.4 (m, 1), 4.0 (d, 1, J = 2.14), 4.99 (d, 1, J = 2.14), 7.35 (m, 5); ^{13}C NMR δ 11.39, 20.91, 29.98, 42.70, 55.31, 71.74, 126.61, 128.79, 129.08, 134.08, 163.42, 199.89; MS m/z 231 (M^+); HRMS calcd for $C_{14}H_{17}NO_2$ 231.1259, found 231.1229.

The oxygenation of **6b** was carried out by means of the procedure described above to give hemiacetal **12** in 56% yield.

4-Hydroxy-6-(4-methoxyphenyl)-2-methyl-4-phenyl-3-oxa-6-azabicyclo[3.2.0]heptane (12): IR (KBr) 1734 (C=O), 3375 (OH) cm^{-1}; ^1H NMR δ 1.47 (d, 3/2, J = 6.83), 1.56 (d, 3/2, J = 6.35), 3.64 (s, 3), 3.68 (m, 1), 4.3 (m, 1/2), 4.45 (d, 1/2, J = 4.09), 4.65 (d, 1/2, J = 4.09), 4.87 (m, 1/2), 6.5–7.5 (m, 9); ^{13}C NMR δ 15.89, 23.55, 55.27, 55.44, 56.69, 57.59, 60.03, 61.35, 64.13, 64.43, 65.42, 71.02, 74.74, 102.65, 103.53, 113.41, 114.36, 117.94, 118.08, 126.69, 126.80, 127.90, 127.95, 128.44, 128.81, 128.88, 130.56, 133.97, 138.34, 155.25, 155.37, 163.49, 164.96; MS m/z 325 (M^+). Anal. Calcd for $C_{19}H_{19}NO_4$: C, 70.14; H, 5.89; N, 4.30. Found: C, 70.27; H, 5.88; N, 4.11.

Acknowledgment. We thank the SC-NMR Laboratory of Okayama University for obtaining the high resolution NMR spectra, and we are grateful for financial support from a Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture, Japan.

Supplementary Material Available: ^1H NMR spectra for all new β-lactams (16 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of this journal, and can be ordered from the ACS; see any current masthead page for ordering information.