Anal. Calcd for $C_{15}H_{25}NO_6$: C, 57.13; H, 7.99; N, 4.44. Found: C, 57.10; H, 7.91; N, 4.42.

In a similar manner **3b** was converted into **5b**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.53 (1 H, d, J = 9 Hz), 4.43 (1 H, d), 3.73 (6 H, s), 2.40–2.20 (2 H, m), 2.04–1.92 (2 H, m), 1.41 (9 H, s).

***cis*-1-(*tert*-Butoxycarbonyl)-2,5-dicarbethoxypyrrolidine (6a).** A solution of 35.4 mg (0.165 mmol, 1.0 equiv) of **4a** and 39.7 mg (0.174 mmol, 1.05 equiv) of Boc_2O in 1.0 mL of MeCN was stirred for 2 h at 23 °C and then evaporated. The residue was dissolved in 10 mL of ether, and the solution was washed with 3 × 2 mL 0.1 M HCl and 1 × 2 mL of brine, dried ($MgSO_4$), and evaporated. The resulting oil was flash chromatographed (1:1 ether/hexane) to yield **6a** as a clear oil, 41.8 mg, 80%: ^{1}H NMR ($CDCl_3$, 250 MHz) δ 4.40 (1 H, t, J = 4.3 Hz), 4.31–4.16 (5 H, m), 2.25–2.09 (4 H, m), 1.42 (9 H, s), 1.30 (3 H, t, J = 6.8 Hz), 1.27 (3 H, t, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 172.2, 171.9, 153.8, 80.9, 61.1, 60.4, 60.2, 29.8, 29.0, 28.5, 14.5, 14.4; TLC R_f 0.51 (7:3 ether/hexane); MS, m/e 315 (M^+), 242 ($M^+ - CO_2Et$), 214 ($M^+ - CO_2tBu$); HRMS; calcd for $C_{15}H_{25}NO_6$ 315.16818, found 315.16795.

In a similar manner **4b** was converted into **6b**: ^{1}H NMR ($CDCl$, 300 MHz) δ 4.43 (1 H, br s), 4.30 (1 H, br s), 3.76 (6 H, s), 2.28–2.10 (4 H, m), 1.43 (9 H, s).

Hydrolysis Experiments with 5b and 6b. Preliminary hydrolysis kinetics were followed at 23 °C in 4:1 methanol–water containing lithium hydroxide and a trace of (benzyloxycarbonyl)glycine as an internal HPLC standard. Disappearance of starting material was followed for 60–70% of the reaction by acid quench, followed by HPLC analysis. In a typical experiment, 94.0 mg (0.33 mmol) of **5b** and 2.1 mg of Z-Gly-OH in 9.8 mL of 4:1 methanol–water was treated with 15.6 mg (0.371 mmol) of $LiOH·H_2O$. Data were taken at 30–40-min intervals, and half-times of 160 and 90 min were observed for **5b** and **6b**, respectively. Treatment of 0.18 mmol each of **5b** and **6b** in 1.2 mL of 4:1 methanol–water with 0.18 mmol of LiOH for 4 h gave after extractive workup an 11% recovery of a 77:23 mixture of 5b:6b. Products of hydrolysis were determined by HPLC, using the known retention times of the monoesters and assigning the diacid structures corresponding to **5b** and **6b** to peaks formed after prolonged reaction time.

***cis*- and *trans*-1-Cyano-2,5-dicarbethoxypyrrolidines (7a and 8a).** The same general procedure[12] was followed for both isomers. To a 1.0 M solution of 2 equiv of **3** or **4** in dry MeCN was added 1 equiv of 5 M BrCN in MeCN; after 24 h the product was isolated by evaporation, solution in CH_2Cl_2, washing with 3 × 8 mL of 0.1 M HCl and 1 × 8 mL of brine, drying, and evaporation.

For **7a**, 354 mg (1.65 mmol) of **3a** yielded a solid that was subjected to flash chromatography (3:2 ether/hexane) to yield 154 mg, 80%, of **7a**: mp 75–77 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.40 (2 H, d, J = 6.6 Hz), 4.26 (4 H, q, J = 7.2 Hz), 2.28–2.10 (4 H, m), 1.32 (6 H, t, J = 7.2 Hz); IR ($CHCl_3$) 2226, 1774 cm^{-1}; TLC R_f 0.76 (ether).

Anal. Calcd for $C_{11}H_{16}N_2O_4$: C, 54.99; H, 6.71; N, 11.66. Found: C, 54.91; H, 6.75; N, 11.62.

For **8a**, 326 mg (152 mmol) of **4a** yielded 152 mg, 86%, of an oil after flash chromatography (7:3 ether/hexane): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.30–4.24 (6 H, m), 2.26–2.22 (4 H, m), 1.32 (6 H, t, J = 7.2 Hz); IR ($CHCl_3$) 2224, 1740 cm^{-1}; TLC R_f 0.62 (ether).

Anal. Calcd for $C_{11}H_{16}N_2O_4$: C, 54.99; H, 6.71; N, 11.66. Found: C, 54.86; H, 6.88; N, 11.83.

***trans*-1-[[(*tert*-Butoxycarbonyl)oxy]carbonyl]-2,5-dicarbethoxypyrrolidine (9a).** A mixture of 37.3 mg (0.175 mmol, 1.05 equiv) of **3a** and 0.5 mg (0.02 equiv) of DMAP was added to a stirred solution of 36.5 mg (0.167 mmol, 1.0 equiv) Boc_2O in 1 mL dry MeCN. After 30 min at 23 °C, the solvent was evaporated, and the residue was dissolved in 10 mL of ether. The solution was washed with 3 × 2 mL of pH 3.5 citrate buffer and 1 × 2 mL of brine, dried ($MgSO_4$), filtered, and evaporated to give 50.2 mg of crude product, 95%. Immediate flash chromatography (3:2 ether/hexane) yielded 33.7 mg (64%) of **9a** as a clear oil that decomposes relatively rapidly at 23 °C: ^{1}H NMR ($CDCl_3$, 250 MHz) δ 4.57 (2 H, t, J = 8.2 Hz), 4.28–4.14 (4 H, m), 2.44–2.24 (2 H, m), 2.14–2.00 (2 H, m), 1.51 (9 H, s), 1.32–1.24 (6 H, m); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 171.7, 171.5, 148.5, 146.7, 85.4, 62.0, 61.9, 60.5, 60.4, 29.5, 28.5, 27.8, 14.5; IR ($CHCl_3$) 1802, 1740 cm^{-1}; TLC R_f 0.49 (7:3 ether/hexane).

Anal. Calcd for $C_{16}H_{25}NO_8$: C, 53.47; H, 6.96; N, 3.90. Found: C, 53.37; H, 6.75; N, 4.05.

Acknowledgment. Financial support from the National Science Foundation (NSF Grant 8116986) and from Pfizer, Inc. is gratefully acknowledged. We are grateful to Dr. Tsutomu Katsuki for communicating his findings to us. We thank Edward Takach of the M.I.T. Chemistry Department Spectrometry Laboratory for mass spectra.

Registry No. **1a**, 50990-24-4; **1b**, 116836-61-4; **2a**, 52321-06-9; **2b**, 102508-03-2; **3a**, 50990-25-5; **3b**, 116836-62-5; **4a**, 90514-00-4; **4b**, 116836-63-6; **5a**, 116724-75-5; **5b**, 116724-76-6; **5b** (diacid), 116724-77-7; **6a**, 116724-78-8; **6b**, 116724-79-9; **6b** (diacid), 116724-80-2; **7a**, 116724-81-3; **8a**, 116724-82-4; **9a**, 116724-83-5.

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Palladium(2+)-Catalyzed Intramolecular Aminocarbonylation of 3-Hydroxy-4-pentenylamines and 4-Hydroxy-5-hexenylamines

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Received August 10, 1988

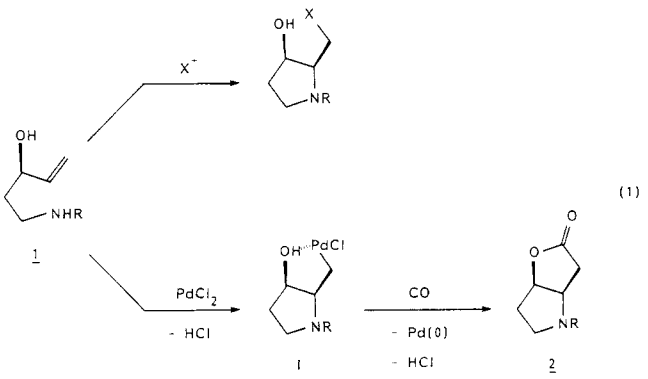
Palladium(2+) salt, in the presence of $CuCl_2$ as an oxidant, catalyzes an intramolecular aminocarbonylation of N-protected 3-hydroxy-4-pentenylamines under 1 atm of carbon monoxide and selectively provides *cis*-3-hydroxypyrrolidine-2-acetic acid lactones. N-Protected 4-hydroxy-5-hexenylamines undergo a similar cyclization; however, in these cases, *cis*- and *trans*-3-hydroxypiperidine-2-acetic acids are formed nonstereoselectively. As an N-protecting group, urea serves as the most reactive and versatile nitrogen nucleophile. Carbamate is more reactive than sulfonamide. The dependence of diastereoselectivity for the cyclization is discussed in terms of the kinds of N-protecting groups, solvents, and electrophiles (Pd^{2+} vs Hg^{2+}, halogens, etc.).

Development of new methodologies for the stereoselective synthesis of multifunctionalized nitrogen heterocycles is a current strong concern of organic chemists because of increasing demands for the syntheses of physio-

0022-3263/88/1953-5731$01.50/0

logically important alkaloids and related compounds.

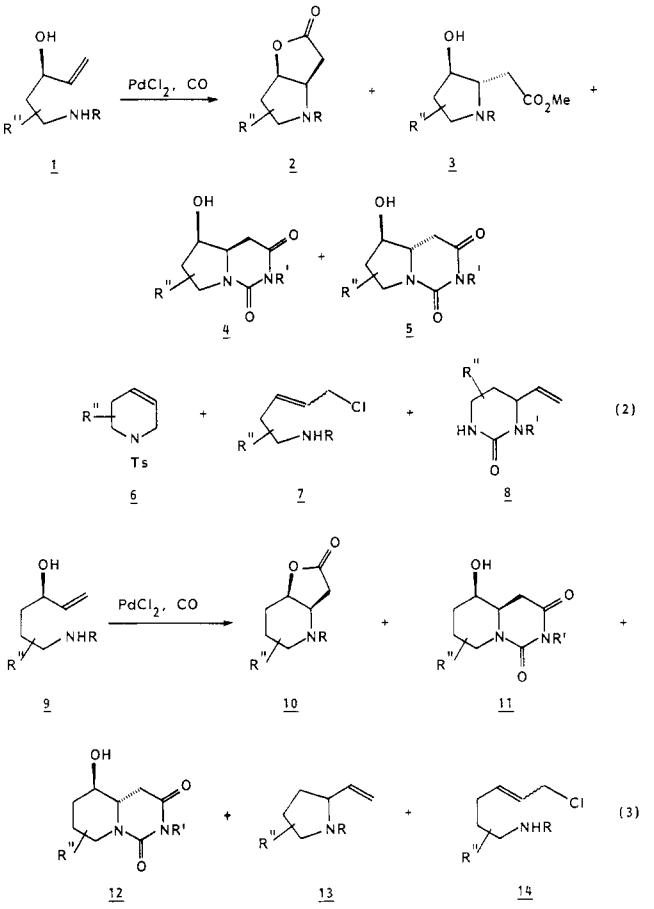
As one of such methodologies, we recently developed a highly stereoselective cyclization of 3-hydroxy-4-pentenylamines 1,[1] which upon exposure to halogenating agents provide *cis*-2-(halomethyl)-3-hydroxypyrrolidines generally in more than 95% selectivity (eq 1, upper).



(1)

We reasoned that the above reaction, with Pd^{2+} substituted for halogenating agents, might stereoselectively provide *cis*-2-(palladiomethyl)-3-hydroxypyrrolidine I as an intermediate, which then undergoes carbonylation and intramolecular esterification to give *cis*-3-hydroxypyrrolidine-2-acetic acid lactone **2** (eq 1, lower). The product **2** is a useful synthetic intermediate for pyrrolizidine alkaloids.[2] However, the success of reaction 1 primarily depends on the diastereoselectivity for the electrophilic addition of Pd^{2+} to the olefin of asymmetric allylic alcohols 1. It is well established that for this type of reaction, especially forming five-membered heterocycles, electrophiles of representative elements show very high stereoselectivities.[3] However, only little is known about the diastereoselectivity for the cyclization with transition-metal electrophiles.[4] The allylic alcohol moiety is labile against Pd^0 species, and hence the stability of this functional group should also be considered, because the aimed palladium(2+)-catalyzed aminocarbonylation produces Pd^0 species after completion of one catalytic cycle of the reaction (eq 1, lower).

This is a full account of our previous paper[5] and focused on the clarification of the scope of the methodology based on the palladium(2+)-catalyzed aminocarbonylation for the syntheses of *cis*-3-hydroxypyrrolidine-2-acetic acid lactones **2** and *cis*-3-hydroxypiperidine-2-acetic acid lactones **10** using 3-hydroxy-4-pentenylamines 1 and 4-hydroxy-5-hexenylamines **9**, respectively, as the starting materials (eq 2 and 3).



(2)

(3)

Results and Discussion

Our recent study on the palladium(2+)-catalyzed intramolecular aminocarbonylation of unsaturated amines[6] revealed that (1) pyrrolidine-2-acetic acids and piperidine-2-acetic acids could be obtained in good yields from N-protected 4-pentenylamines and 5-hexenylamines, respectively; (2) as an N-protecting group, urea [(alkylamino)carbonyl and (arylamino)carbonyl] is most reactive and versatile; carbamate (alkoxycarbonyl) is more reactive than sulfonamide (tolylsulfonyl); (3) protic solvents, especially acetic acid containing sodium acetate, are superior to aprotic solvents like tetrahydrofuran and dichloromethane.

On the basis of information, we examined aminocarbonylation of N-protected 3-hydroxy-4-pentenylamines **1** and 4-hydroxy-5-hexenylamines **9**[7] in the expectation of the selective formation of *cis*-3-hydroxypyrrolidine-2-acetic acid lactones **2** (eq 2) and *cis*-3-hydroxypiperidine-2-acetic acid lactones **10** (eq 3), respectively.

Seven kinds of 3-hydroxy-4-pentenylamines **1a–g** and four kinds of 4-hydroxy-5-hexenylamines **9a–d** were examined, with variation of the kinds of N-protecting groups. Generally, aminocarbonylation was carried out in a 1-mmol scale of **1** or **9** by using 0.1 mmol (10 mol %) of $PdCl_2$ and 3 mmol of $CuCl_2$ at ambient temperature and under an ambient pressure of carbon monoxide in three different kinds of solvents: methanol (5 mL), acetic acid (5 mL,

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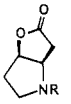
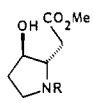
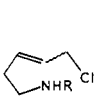
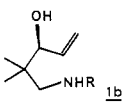
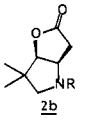
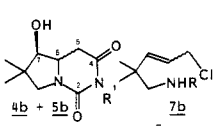
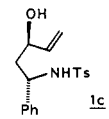
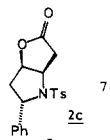
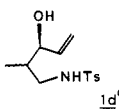
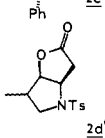
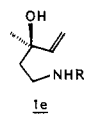
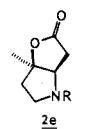
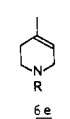
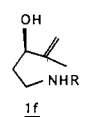
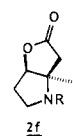
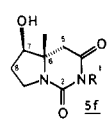
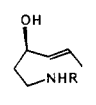
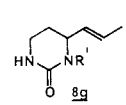
(6) Tamaru, Y.; Hojo, M.; Higashimura, H.; Yoshida, Z. *J. Am. Chem. Soc.* **1988**, *110*, 3994.

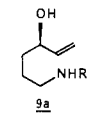
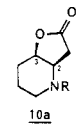
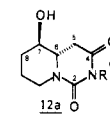
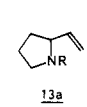
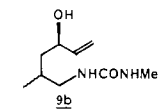
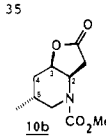
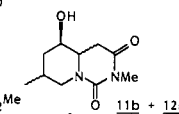
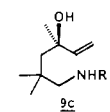
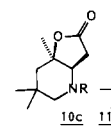
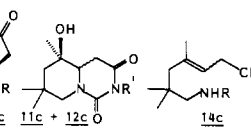
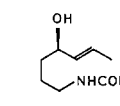
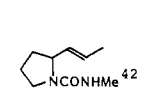
(7) Racemic alcohols are used. For the sake of simplicity, only one enantiomer is shown in equations and tables.

Table I. Palladium(2+)-Catalyzed Aminocarbonylation of N-Protected 3-Hydroxy-4-pentenylamines

entry	substrate	condtns[a] (day)	products % yield (% convrsn)[b] [product ratio]		
					
	1a		2a	3a	7a
1	R = SO_2Tol	MeOH (1)	37	10	43
2		AcOH (1)	90	0	0
3	R = CO_2Me	MeOH (1)	35	0	24
4		AcOH (2)	95	0	0
5		THF (2)	<10	0	0
6	R = CONHPh	AcOH (2)	66	0	0
					
	1b		2b	4b + 5b	7b
7	R = CO_2Me	MeOH (1)	70		5
8	R = CONHMe	MeOH (1)	33	67 [1:1]	
9		AcOH (2)	75	17 [1:1]	
10	R = CONHPh	MeOH (1)	97	0	0
11		AcOH (2)	85	0	0
					
12		AcOH (2)			74 (93)
	1c		2c		
					
13		AcOH (2)			70
	1d[c]		2d[c]		
					
	1e		2e	6e	
14	R = SO_2Tol	AcOH (1)	66	30	
15	R = CO_2Me	AcOH (2)	79	0	
16	R = CONHMe	AcOH (2)	42	0	
17	R = CONHPh	AcOH (2)	71	7	
					
	1f		2f	5f	
18	R = SO_2Tol	AcOH (2)	0 (0)		
19	R = CO_2Me	AcOH (3)	28 (35)		
20	R = CONHMe	AcOH (2)	46	23	
21	R = CONHPh	MeOH (1)	complex mixture		
22		AcOH (3)	44		
					
	1g		8g		
23	R = SO_2Tol	AcOH (3)	0 (0)		
24	R = CO_2Me	AcOH (3)	0 (0)		
25	R = CONHMe	MeOH (2)	90		
26	R = CONHPh	MeOH (1)	90		

[a] Compound 1 (1 mmol), $PdCl_2$ (0.1 mmol), $CuCl_2$ (3 mmol), and CO (1 atm) at ambient temperature in either dry methanol (5 mL), tetrahydrofuran (THF, 5 mL), or acetic acid (5 mL, containing 3 mmol of sodium acetate). [b] If not specified, the conversion is 100%. [c] Diastereomeric mixture, 1:1.

Table II. Palladium(2+)-Catalyzed Aminocarbonylation of N-Protected 4-Hydroxy-5-hexenylamines

entry	substrate	condtns[a] (day)	products % yield (product ratio)		
					
	9a		10a	12a	13a
1	R = SO_2Tol	AcOH (2)	0	0	84
2	R = CO_2Me	AcOH (2)	0	0	74[b]
3	R = CONHMe	AcOH (2)	22	26	
4	R = CONHPh	AcOH (2)	35		
					
	9b		10b	11b + 12b	
5		AcOH (4)	14	32[d]	
					
	9c		10c	11c + 12c	14c
6	R = CONHMe	AcOH (3)	34	13 (2:3)	15
7	R = CONHPh	AcOH (3)	33	0	7[c]
					
8		AcOH (3)			42
	9d		13d		

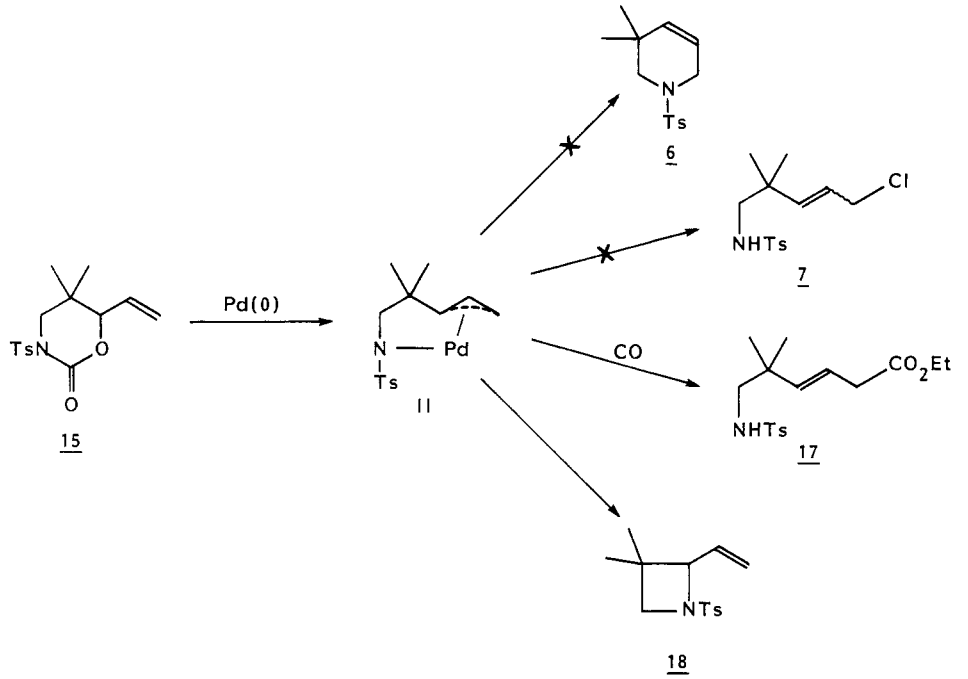
[a] The conditions are the same as those in Table I. [b] *N*-(Methoxycarbonyl)-6-acetoxyl-4-hexenylamine is isolated in 7% yield. [c] *N*-[(Phenylamino)carbonyl]-2,2,4-trimethyl-6-acetoxy-4-hexenylamine is isolated in 5% yield. [d] The products **11b** and **12b** were tentatively assigned on the basis of IR (1715, 1660 cm^{-1}) and ^1H NMR (*N*-methyl singlet) spectra. These (possibly four) isomers could not be purified by means of column chromatography.

containing 3 mmol of sodium acetate), or tetrahydrofuran (THF, 5 mL). Results are summarized in Tables I and II. For the sake of simplicity, the relative amounts of reagents and solvents were kept constant, as indicated above, all through the reactions listed in Tables I and II. The amount of palladium chloride catalyst may be significantly reduced. For instance, the reaction of **1b** (R = CONHPh, 2.3 mmol) with 0.023 mmol (1 mol %) of $PdCl_2$ and 6.9 mmol of $CuCl_2$ in AcOH (11.5 mL)–AcONa (6.9 mmol) under 1 atm of CO at room temperature for 7 days gave **2b** (R = CONHPh) in 92% isolated yield (cf. entry 11, Table I).

In accordance with our previous observation,[6] the reaction largely depends on the reaction media. Acetic acid is the best choice of the solvents. In methanol, the reaction sometimes suffers from low stereoselectivity (**2** vs **3** and **2** plus **4** vs **5**; entries 1 and 8, Table I, vide infra). Furthermore, this solvent tends to cause side reactions, giving 5-chloro-3-pentenylamines **7** (entries 1, 3, and 7, Table I) and/or many unidentified products (entry 21, Table I).

In THF, the reaction was unacceptably slow (entry 5, Table I). In order to complete the reaction, we examined stoichiometric reactions: e.g., a mixture of $PdCl_2(CH_3CN)_2$ (1 mmol) and **1a** (R = CO_2Me, 1 mmol) in dry THF under 1 atm of carbon monoxide formed a copious purple precipitate, which after aqueous workup only furnished the starting **1a**. Treatment with triethylamine (4 mmol) was effective to promote the cyclization. However, the conversion was still low (ca. 50%). When 2 equiv of $PdCl_2(CH_3CN)_2$ was used, the reaction attained completion and **2a** (R = CO_2Me) could be isolated in 50% yield. These

Scheme I



results are in marked contrast to those of a stoichiometric reaction in methanol, which proceeds smoothly in the absence of triethylamine and provides **2a** (R = CO_2Me) in 85% yield (1 equiv of $PdCl_2$ under 1 atm of CO).

As far as the aminocarbonylation of **1** is concerned, carbamate and urea could be utilized with similar effectiveness. Tolylsulfonyl is an attractive protecting group, because sulfonamides are usually stable crystalline solids and easy to purify and handle. However, they show somewhat reduced reactivity (entry 14, Table I), and in some cases they were unreactive and recovered completely (entry 18, Table I).

Compared with 3-hydroxy-4-pentenylamines **1**, 4-hydroxy-5-hexenylamines **9** are much less reactive. In this case, sulfonamide and carbamate are completely ineffective and only provide a substitution product **13** (entries 1 and 2, Table II). Only urea serves as a nitrogen nucleophile toward aminocarbonylation (entries 3 and 4, Table II).

We sometimes encounter the fact that the reactions forming five-membered rings are not necessarily applicable to the synthesis of six-membered rings.[1b,8] Haloamidation of **1a** and **9a** (R = SO_2Tol and CO_2Me) is just one of such cases.[1b] The former, **1a**, readily undergoes cyclization and provides *cis*-2-(halomethyl)-3-hydroxypyrrolidine in high yield (eq 1, upper), while the latter, **9a**, is either unreactive or provides many unidentified products under similar halogenation conditions. In this context, it is our delight to find that compounds **9**, though only when the amino group is protected as urea, undergo the aminocarbonylation and furnish piperidine lactones **10** and their derivatives **11** and **12** (eq 3). Reaction 3 somehow owes its success to a specific nucleophilic affinity of urea toward the olefins activated by the coordination of Pd^{2+}, since we are not successful yet in the haloamidation of **9a** (R = CONHMe).

In order to avoid undesirable side reactions, we consider the reaction paths for **6–8**, **13**, and **14**. First, acid catalysis (HCl and/or AcOH) is conceivable, since 2 mol of hydrogen chloride are formed by the conversion of **1** to **2** and **9** to **10** (eq 1). However, a quantitative transformation of **1a** (R = SO_2Tol) to *N*-(tolylsulfonyl)-3-acetoxy-4-pentenylamine (**16**) and no formation of **7a** (3 equiv of concentrated HCl in acetic acid at room temperature for 20 h) seems to eliminate this possibility. As another path, an intermediacy of (π-allyl)palladium II, possibly formed by an oxidative addition of Pd^0 to the allylic C–O bond of **1**, seems probable (Scheme I). In order to mimic the reaction, we generated II from carbamate **15** by Tsuji's decarboxylation method.[9] However, II did not undergo an Endo-Trig substitution to provide **6**, but did undergo an Exo-Trig cyclization to give an azetidine **18** (3 mol % of $Pd(PPh_3)_4$ in ethanol under argon). Under 1 atm of carbon monoxide, it furnished an amino acid ester **17** (3 mol % of $Pd(OAc)_2(PPh_3)_2$ in ethanol). A slight modification of the conditions of eq 1 [$PdCl_2(PPh_3)_2$ (0.05 equiv) and $CuCl_2$ (3 equiv) in dry acetonitrile under 1 atm of CO at ambient temperature] caused a dramatic change of product distribution, and only **7a** (R = SO_2Tol, 67% yield from **1a**) and **6e** (R = SO_2Tol, 37% yield from **1e**) were obtained as isolable products. In these experiments, no aminocarbonylation products **2a** and **2e** were detected. Anyway, cupric chloride must take part, at least, for the formation of **7** and **14** as a chlorine source.[10] Hence, we examined the following chlorine-free catalytic conditions: $Pd(OAc)_2$ (0.1 equiv) and $Cu(OAc)_2$ (3 equiv) in methanol under 1 atm of CO; $Pd(OAc)_2$ (0.1 equiv) and benzoquinone (3 equiv) in methanol under 1 atm of CO. These reactions, however, provided neither the carbonylation product **2a** nor the substitution products, just resulting in the recovery of the starting **1a** (R = SO_2Tol). On the basis of these experiments, we were unable to specify the paths for the side reactions; however, the results obtained in these experiments seem to involve some important findings concerning the azetidine formation and the chlorination of allylic alcohols (Scheme I). These subjects will be dealt with elsewhere.

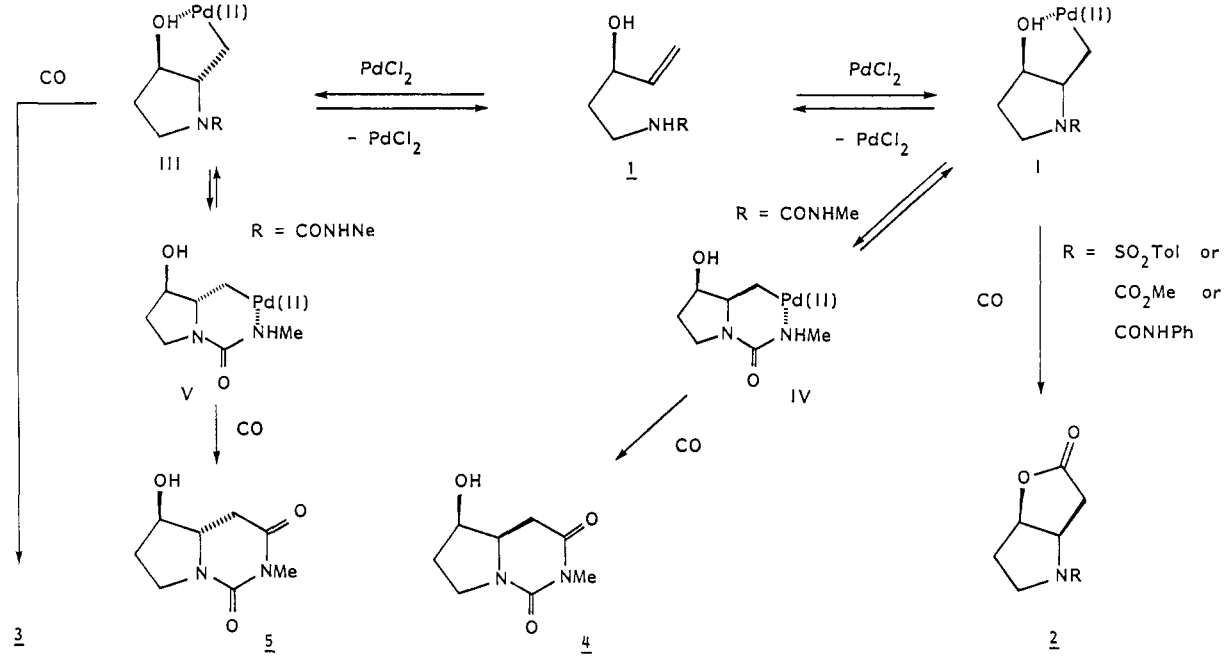
Close examination of the results listed in Table I reveals some interesting features. As for the reactivity, the C_1–C_3-substituted hydroxy amines **1b–e** react with similar

(8) Hegedus, L. S.; McKearin, J. M. *J. Am. Chem. Soc.* **1982**, *104*, 2444.

(9) (a) Tsuji, J. *Tetrahedron* **1986**, *42*, 5361. (b) Tamaru, Y.; Bando, T.; Hojo, M.; Yoshida, Z. *Tetrahedron Lett.* **1987**, *28*, 3497.

(10) Bäckvall, J.-E. *Acc. Chem. Res.* **1983**, *16*, 335.

Scheme II



ease to the parent **1a**. The smooth and high-yield cyclization of the quarternary substrate **1e** should be noted. The C_4- and C_5-substituted ones (**1f** and **1g**) show apparently reduced reactivities. Especially **1g**, with a methyl substituent on the terminal olefinic carbon, was totally unreactive toward aminocarbonylation, and it was either converted to a substitution product, 3,4,5,6-tetrahydro-2-(1*H*)-pyrimidinone **8g**, or recovered. This is in contrast to a successful aminocarbonylation of *trans*- and *cis*-4-hexenylamines, previously reported from these laboratories.[6]

As for the stereoselectivity, the present Pd^{2+}-promoted aminocarbonylation shows, in some cases, rather poor cis selectivity as compared with that for the cyclization with representative elements.[3] For example, iodoamidations[1a] of **1a**, **1b**, and **1f** provide *cis*-2-(iodomethyl)-3-hydroxypyrrolidines in 95%, 95%, and 93% selectivities, respectively. The low selectivities are commonly observed in the cases where the reactions are conducted in methanol (entry 1, Table I) and/or the amino group is protected as *N*-methylurea (entries 8, 9, and 20, Table I). Impressively, in the case of entry 8, Table I, the trans-cyclization product, (6*S**,7*R**)-3,8,8-trimethyl-7-hydroxy-1,3-diazabicyclo[4.3.0]nonane-2,4-dione (**5b**), is obtained in so much as 33% yield and the cis selectivity is as low as 67% (**2b** + **4b**)! The high cis selectivity is recovered when the reaction is carried out in acetic acid (entry 9). In the case of entry 20, the cis selectivity is similarly poor (67%), even for the reaction in acetic acid.

All these results indicate that *palladium(2+) is a poor electrophile with respect to diastereoselectivity for the aminocyclization of I and kinetically provides a mixture of cis- (I) and trans-3-hydroxy-2-(palladiomethyl)-pyrrolidines (III) nonselectively* (Scheme II).

The apparent high cis selectivities, especially for those reactions undertaken in acetic acid, may be attributed to the result of an equilibrium between I and III, where the cis isomer I may be more stable than the trans isomer III owing to a coordination of the hydroxyl group to Pd^{2+}. In acetic acid, the equilibrium may be attained owing to its low nucleophilicity and also owing to its acidity, with which, through protonation to urea, the urea may be divested of the coordination ability to form IV and V. The differences in the thermodynamic stabilities between these intermediates may be so small that a 1:1 mixture of *cis*- and *trans*-hydroxydihydrouracils, **4** and **5**, may result (entries 8 and 9). The formation of trans isomer **3** may be attributed to the high nucleophilicity of methanol, with which the equilibrium between I and III is intercepted before its completion (entry 1, Table I).

Hitherto, the diastereoselectivity for the electrophilic addition to chiral allylic alcohols has been accounted for on the basis of the relative abundances and reactivities of their conformers as well as the position of a transition state in the reaction coordinate,[11] and no attention has been paid to the kinds of electrophiles. However, the results mentioned above clearly indicate that consideration of the kind of electrophile is required for a better understanding of the diastereoselection.[12]

Although the number of examples is limited, it may be safely said that the palladium-catalyzed aminocyclization forming piperidines is less stereoselective than that forming pyrrolidines (Table II). To our knowledge, only four reports have appeared for the Exo-Trig cyclization of chiral allylic alcohols forming six-membered heterocycles.[4b,13] Two of them show that seleno-[13a] and mercurioetherification[13b,c] of 4-(benzyloxy)-5-hexenyl alcohols are highly stereoselective and exclusively provide *cis*-2-(sele-

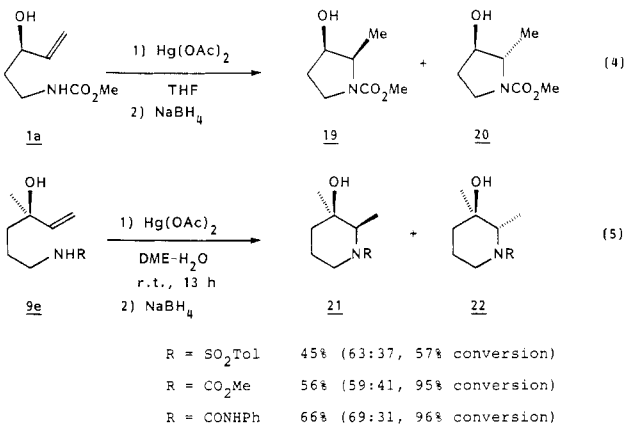
(11) (a) Kahn, S. D.; Hehre, W. J. *Tetrahedron Lett.* **1985**, *26*, 3647. (b) Kahn, S. D.; Pau, C. F.; Hehre, W. J. *J. Am. Chem. Soc.* **1986**, *108*, 7396. (c) Kahn, S. D.; Hehre, W. J. *Ibid.* **1987**, *109*, 666. (d) Chamberlin, A. R.; Mulholland, R. L.; Kahn, R. L., Jr.; Hehre, W. J. *Ibid.* **1987**, *109*, 672.

(12) Although we are unable to clarify the stereochemistry of the aminopalladation on olefin (whether cis or trans addition), owing to a low reactivity of terminally substituted 1 (e.g., **1g**), we have already verified that aminopalladation takes place stereospecifically in a trans fashion by using *cis*- and *trans*-*N*-[(phenylamino)carbonyl]-4-hexenylamines as probes.[6] See also: Åkermark, B.; Zetterberg, K. *J. Am. Chem. Soc.* **1984**, *106*, 5560. These results seem to indicate that the reaction mechanism of the aminopalladation is very similar to the other cyclizations with representative elements[3,11] and hence that there seems to be no necessity for considering any specific interaction between Pd^{2+} and urea, which might alter the diastereoface selection.

(13) (a) Lancelin, J.-M.; Pougny, J.-R.; Sinaÿ, P. *Carbohydr. Res.* **1985**, *136*, 369. (b) Pougny, J.-R.; Nassr, M. A. M.; Sinaÿ, P. *J. Chem. Soc., Chem. Commun.* **1981**, 357. (c) Nicotra, F.; Ronchetti, F.; Russo, G. *Ibid.* **1982**, 470. (d) Bernotas, R. C.; Ganem, B. *Tetrahedron Lett.* **1985**, *26*, 1123.

nomethyl)- and *cis*-2-(mercuriomethyl)-3-(benzyloxy)-tetrahydropyrans, respectively. Oxycarbonylation of 5-hexene-1,4-diols with a stoichiometric amount of $Pd(OAc)_2$ furnishes *cis*-3-hydroxytetrahydropyran-2-acetic acid lactones in 100–83% selectivities.[4b] On the other hand, the fourth study, which deals with a mercurioamination of 4-(benzyloxy)-5-hexenylamines, indicates that the stereoselectivity is incoherent and subtly affected by substitution patterns of the substrates, providing either *cis*- or *trans*-2-(mercuriomethyl)-3-(benzyloxy)piperidines as major products.[13d] The stereoselectivity of the last example seems to coincide with our observations (Table II).

We examined Hg^{2+} as a reference metal electrophile to Pd^{2+} and found that aminomercuriation of **1** and **9** shows similar stereoselectivities to those of the aminopalladation, providing *cis*-pyrrolidine **19** selectively (eq 4) and a random mixture of *cis*- and *trans*-piperidines **21** and **22**, whose relative configuration is not determined yet (eq 5). Thus,



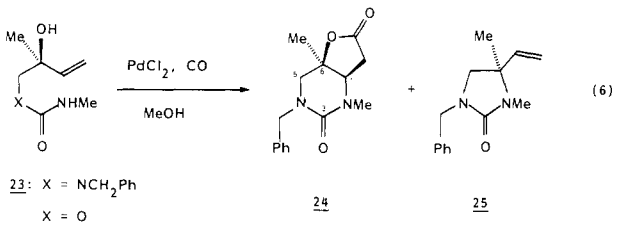
exposure of **1a** to 1.1 equiv of mercuric acetate in THF, followed by reduction with $NaBH_4$, provided *cis*- (**19**) and *trans*-3-hydroxy-2-methylpyrrolidines (**20**) in a 91:9 ratio in 85% yield (eq 4). An authentic sample of the trans isomer **20** was prepared by Mitsunobu inversion[14] of the cis isomer **19**. Aminomercuriation can be successfully applied to the relatively unreactive **1f** (R = CO_2Me), and *N*-(methoxycarbonyl)-2,2-dimethyl-3-hydroxypyrrolidine was obtained in 85% yield. Under the above conditions, **9e** is unreactive. For the promotion of the cyclization, the presence of water is essential. Interestingly, here again, the relative reactivity decreases in the order urea ≥ carbamate > tosylamide, as judged from the conversions of the reactions under the same conditions (eq 5).

The structure determination of the products obtained in the series of the present experiments is as follows. The cis-fused bicyclic [3.3.0] skeleton **2** is consistent with the standard carbonyl absorptions of butyrolactone in the IR spectra (ca. 1780 cm^{-1}). The trans configuration **3** is deduced from the fact that it does not undergo an intramolecular esterification; otherwise, butyrolactone is a more stable form than the hydroxy ester form. Owing to a fluxional nature of the conformation of the pyrrolidine ring, no reliable standards for the relative configuration around C_2 and C_3 could be obtained on the basis of the $J_{C_2HC_3H}$ values in ^1H NMR spectra. In these cases, NOE experiments turned out most convincing.[15] For example, a significant increase of the area intensity of one of the methylene protons of the 2-acetic acid group, caused by irradiation at the *CH*(OH) proton, concludes that **3a** is trans substituted. Similarly, the stereochemistry of **5f** was deduced on the basis of the following observations: Irradiations at C_6Me and C_7H, respectively, cause significant increases of area intensities of one of the other of the C_5 and C_8 methylene protons, while no NOE is observed between C_6Me and C_7H.

A mixture of **4b** and **5b** (R′ = Me) was not separable by means of column chromatography and showed a very complex ^1H NMR spectrum, from which no structural information could be drawn. Their bicyclic [4.3.0] skeletons were concluded on the basis of the following oxidation–reduction sequence: an oxidation with $CrO_3(pyridine)_2$, giving 3,8,8-trimethyl-1,3-diazabicyclo[4.3.0]nonane-2,4,7-trione as a single isomer (1760, 1710, 1665 cm^{-1}), and a reduction ($NaBH_4$, in ethanol), giving a 7:3 mixture of **4b** and **5b**.

Although **10a** shows halfway values [$J_{C_2HC_3H}$ = 7.3 Hz (R = CONHPh), 6.8 Hz (R = CONHMe)] as typical diaxial and axial–equatorial coupling constants of cyclohexane derivatives, the cis skeleton of **10a** (R = CONHPh) was determined on the basis of the typical coupling constant observed for the aminolysis product [*cis*-*N*-[(phenylamino)carbonyl]-2-[[(methylamino)carbonyl]methyl]-3-hydroxypiperidine, $J_{C_2HC_3H}$ = 5.9 Hz]. The structural proof of **10b**, obtained as a single lactone from a 1:1 mixture of diastereomers **9b**, relies on the coupling patterns of the H_{4a} proton (ddd, *J* = 14.9, 11.5, and 3.4 Hz), where the coupling constants $J_{H_{4a}H_{3a}}$ = 3.4 and $J_{H_{4a}H_{5a}}$ = 11.5 Hz indicate the axial C_3–O and equatorial C_5–Me orientations. The 6*S**,7*R** configuration of **12a** (R′ = Me) was deduced on the basis of $J_{C_6HC_7H}$ = 9.7 Hz and a positive NOE between H_{5a} and H_7 (see Experimental Section).

As an extension of reaction 3, we examined an aminocarbonylation of **23** (eq 6). Urea **23** (X = NCH_2Ph) undergoes a smooth aminocarbonylation under the usual conditions, and in this case the cis lactone **24** was produced specifically in 68% isolated yield together with a small amount of imidazolidinone **25** (9%). This apparent cis-



selective aminocarbonylation might be ascribed to a reversible nature of aminopalladation as described before[16] (Scheme II). The cis lactone structure of **24** was concluded on the basis of differential NOE experiments: C_1H (+8.7%), one proton of C_5H_2 (+4.9%), and the other proton of C_5H_2 (+0.8%) by irradiation at C_6Me. The corresponding carbamate **23** (X = O), on the other hand, was unreactive and recovered completely. These contrasting results further seem to support a general trend that urea is more reactive than carbamate toward palladium-catalyzed aminocarbonylation.

The utility of the present aminocarbonylation may be apparent from the structures of a series of products. The pyrrolidine lactone **2a** has long been known as a Geissman–Waiss lactone[2b] and has been utilized as a versatile intermediate for the synthesis of many pyrrolizidine alkaloids. This lactone **2a** was originally prepared in 32% overall yield in four steps starting from β-alanine and diethyl fumarate.[2b] The same lactone, according to our

(14) Mitsunobu, O. *Synthesis* **1981**, 1.
(15) Gaudemer, A. *Determination of Configuration by NMR Spectroscopy* in *Stereochemistry*; Kagan, H. B., Ed.; Georg Thieme: Stuttgart, 1977; Vol. 1, Chapter 2.
(16) Bäckvall, J.-E.; Björkman, E. E. *Acta Chem. Scand., Ser. B* **1984**, *B38*, 91.

procedure, was obtained in 85% overall yield in the same four steps: addition of lithioacetonitrile to acrolein, reduction of the thus-obtained cyano alcohol with lithium aluminum hydride to hydroxylamine, and N-protection, followed by the present aminocarbonylation. The other **2** and **10** may also be used as the intermediates for the syntheses of pyrrolizidine and lycopodium alkaloids.[2a] Reaction 6 is attractive particularly in view of a current interest in the synthesis of unusual amino acids. The usefulness of the present methodology may be further augmented by the ease with which the aminocarbonylation can be carried out and the starting amines with a wide structural variety could be prepared. The use of palladium salt in a catalytic amount (0.01–0.10 equiv) may also be an important aspect to be noted, especially from an economical point of view.

Experimental Section

Melting points were determined in capillary tubes with a Büchi apparatus and were not corrected. Unless otherwise specified, short-path (bulb-to-bulb) distillations were carried out in a Kugelrohr apparatus. Microanalyses were performed by the Microanalysis Center of Kyoto University. Infrared spectra were measured with a Hitachi Model EPI-G3 grating spectrophotometer. Proton magnetic resonance spectra were determined either at 90 MHz on a JEOL-FX90Q instrument or at 400 MHz on a JEOL-GX400 instrument with tetramethylsilane as an internal standard. Carbon-13 NMR spectra were determined at 22.4 MHz on a JEOL-FX90Q instrument. Mass spectra were measured on a JEOL D-300 instrument (high-resolution mass spectrophotometer).

Solvents and Reagents. Acetic acid was dried by distillation from acetic acid–benzene. Methanol and ethanol were dried and distilled from magnesium. Tetrahydrofuran, diethyl ether, and benzene were dried and distilled from sodium–benzophenone. All these solvents were distilled and kept under argon and transferred via a syringe. The following reagents (reagent grade) were used without further purification: palladium chloride, cupric chloride, mercuric acetate, carbon monoxide, and sodium acetate.

N-Protected 3-hydroxy-4-pentenylamines 1 and 4-hydroxy-5-hexenylamines 9: compounds 1a–g and 9a–c were prepared according to the procedure reported previously.[1b]

***trans*-N-[(Methylamino)carbonyl]-4-hydroxy-5-heptenylamine (9d).** Into a stirred suspension of Zn–Cu (2.15 g) in dry ether (50 mL) and *N,N*-dimethylacetamide (3.7 mL) was added 3-iodopropionitrile (5.43 g, 30 mmol) under argon, under a gentle reflux (over a 10-min period). After the mixture was stirred for 3 h at ambient temperature, tetrakis(triphenylphosphine)palladium (145 mg, 0.15 mmol) was added in one portion, and then crotonoyl chloride (2.4 mL, 25 mmol) was added over a 10-min period. After being stirred for 2 h at ambient temperature, the mixture was diluted with ether, washed with saturated NaCl and saturated $NaHCO_3$, dried ($MgSO_4$), and condensed. Distillation of the residue gave 2.54 g of *trans*-4-oxo-5-heptenenitrile [83% yield, bp 135 °C (0.5 mmHg)], which was reduced with 1.5 equiv of $LiAlH_4$ (84%), and the thus-obtained hydroxylamine was reacted with methyl isocyanate to give **9d** as described previously.[1b]

***N*-[(Methylamino)carbonyl]-*N*-benzyl-2-methyl-2-hydroxy-3-butenylamine (23, X = NCH_2Ph).** A mixture of 2-methyl-1,3-butadiene 1,2-epoxide (1.6 g, 20 mmol), benzylamine (2.0 g, 20 mmol), and pyridine (2 mL) was heated at 60 °C for 1 week under argon. The resultant mixture was diluted with dichloromethane (20 mL) and cooled to 0 °C. Into this mixture was added methyl isocyanate (1.1 g, 20 mmol) over a 5-min period, and the mixture was stirred overnight at the same temperature. After removal of low-boiling materials under reduced pressure, the residue was chromatographed over silica gel (ethyl acetate as an eluent) to give **23** in 80% overall yield.

2-Methyl-2-hydroxy-3-butenyl *N*-Methylcarbamate (23, X = O). 2-Methyl-1,3-butadiene 1,2-epoxide (0.4 g, 5 mmol) was heated at 60 °C for 20 h in 6 mL of 2.5 N NaOH. After neutralization with 2 N HCl and saturation with NaCl, the mixture was extracted with ether by means of a perforator. Into the mixture, cooled to 0 °C, was added pyridine (0.4 mL, 5 mmol) and methyl isocyanate (285 mg, 5 mmol), and the mixture was stirred overnight. After removal of low-boiling materials, the residue was chromatographed over silica gel (benzene–ethyl acetate, 1:1 v/v) to give **23** in 83% overall yield.

General Procedure for Pd^{2+}-Catalyzed Aminocarbonylation of 1, 9, and 23. A 10-mL, two-necked, round-bottomed flask, containing a magnetic stirring bar, $PdCl_2$ (17.7 mg, 0.1 mmol), and $CuCl_2$ (404 mg, 3 mmol), was fitted with a serum cap and a reflux condenser equipped at the top with a CO balloon. For the reaction using acetic acid as a solvent, NaOAc (246 mg, 3 mmol) was also placed in the flask at this stage. After purging with CO, a solution of **1**, **9**, or **23** in 5 mL of an appropriate solvent (acetic acid, methanol, or tetrahydrofuran) was added and the resultant heterogeneous mixture was stirred at ambient temperature for the period of time indicated in Tables I and II. After removal of the solvent under reduced pressure at ambient temperature, the residue was washed with ethyl acetate and filtered with suction through a Celite pad on a funnel and the filtrate was washed with aqueous $NaHCO_3$. After drying of the extract ($MgSO_4$) and removal of the solvent, the residue was chromatographed over silica gel. Typical R_f values of products (Merck precoated silica gel plate, 60F254) are as follows (ratios in volume): **2a** (R = Ts), 0.5 (hexane–ethyl acetate, 1:1); **2a** (R = CO_2Me), 0.4 (benzene–ethyl acetate, 1:1); **3a** (R = Ts), 0.45 (hexane–ethyl acetate, 1:1); **2b** (R = CONHMe), 0.1 (ethyl acetate); **2b** (R = CONHPh), 0.3 (hexane–ethyl acetate, 1:1); **4b**, **5b** (R = CONHMe), 0.5 (ethyl acetate); **8g** (R = CONHMe), 0.1 (acetone–benzene, 4:1); **8g** (R = CONHPh), 0.1 (ethyl acetate); **10c** (R = CONHMe), 0.5 (ethyl acetate–methanol, 6:1); **11c**, **12c** (R′ = Me), 0.7 (ethyl acetate–methanol, 6:1); **14c** (R = CONHMe), 0.6 (ethyl acetate–methanol, 6:1); **10c** (R = CONHPh), 0.2 (hexane–ethyl acetate, 2:1); **14c** (R = CONHPh), 0.5 (hexane–ethyl acetate, 2:1); **13a** (R = CO_2Me), 0.8 (ethyl acetate); **13d** (R = CONHMe), 0.3 (ethyl acetate); **21**, **22** (R = CO_2Me), 0.62, 0.65 (ethyl acetate); **21**, **22** (R = Ts), 0.53, 0.55 (ethyl acetate); **21**, **22** (R = CONHPh), 0.4 (benzene–ethyl acetate); **24**, 0.1 (ethyl acetate–hexane, 2:1); **25**, 0.5 (ethyl acetate–hexane, 2:1).

Stoichiometric Aminocarbonylation of 1a (R = CO_2Me) in THF. Into a flask containing $PdCl_2(CH_3CN)_2$ (249 mg, 1 mmol), purged with CO (a balloon), was added a solution of **1a** (0.5 mmol) in 10 mL of dry THF at 0 °C. After stirring for 30 min at 0 °C, triethylamine (0.278 mL, 2 mmol) was added in four portions (0.5 mmol each) at 10-min intervals, during which the color of the mixture turned from purple to yellow and then to black. The mixture was stirred for an additional 2 h, then diluted with ether, and filtered through a Celite pad. Evaporation of the solvents and purification by silica gel column chromatography (benzene–ethyl acetate, 1:1 v/v) gave **2a** (R = CO_2Me) in 50% yield.

***cis*-N-(Tolylsulfonyl)-3-hydroxypyrrolidine-2-acetic acid lactone (2a, R = SO_2Tol)**: mp 133.0–134.0 °C (benzene–hexane); IR (KBr disk) 1770 (s), 1335 (s), 1155 (s), 1090 (m), 975 (m), 715 (m), 655 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.6–2.3 (m, 2 H), 2.44 (s, 3 H), 2.86–2.93 (m, 2 H), 3.42–3.60 (m, 2 H), 4.35 (dt, J = 5.1, 2.9 Hz, 1 H, coalescing to d, J = 5.1 Hz, by irradiation at 2.9), 5.00 (dt, J = 5.1, 1.7 Hz, 1 H), 7.34 (d, J = 8.3 Hz, 2 H), 7.71 (d, J = 8.3 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 30.8 (C_4), 36.6 (CH_2CO), 21.3 (Me), 46.7 (C_5), 59.9 (C_2), 83.1 (C_3), 174.6 (CO). Anal. Calcd for $C_{13}H_{15}NO_4S$: C, 55.50; H, 5.37; N, 4.98; S, 11.40. Found: C, 55.37; H, 5.44; N, 5.00; S, 11.51.

***cis*-N-(Methoxycarbonyl)-3-hydroxypyrrolidine-2-acetic acid lactone (2a, R = CO_2Me)**: mp 84.0 °C (ether); IR (KBr disk) 1780 (v), 1690 (s), 1455 (s), 1400 (s), 1235 (m), 1165 (m), 1115 (m), 1030 (m), 990 (m), 765 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz, 60 °C) δ 2.04 (dddd, J = 4.6, 9.3, 11.0, 14.1 Hz, 1 H), 2.30 (dd, J = 6.3, 14.1 Hz, 1 H), 2.79 (br s, half-width = 10 Hz, 2 H), 3.40 (dt, 6.3, 11.0 Hz, 1 H), 3.72 (s, 3 H), 3.78 (br s, 1 H), 4.48 (dd, J = 4.0, 4.6 Hz, 1 H), 5.06 (t, J = 4.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 60 °C) δ 30.5 (C_4), 35.8 (CH_2CO), 44.2 (C_5), 52.4 (Me), 58.0 (C_2), 83.1 (C_3), 154.6 (NCO), 174.9 (CO); high-resolution mass spectrum calcd for $C_8H_{11}NO_4$ 185.0696, found m/z (relative intensity) 185.0697 (100), 170 (25), 167 (20), 148 (85), 129 (40), 126 (50).

***cis*-N-[(Phenylamino)carbonyl]-3-hydroxypyrrolidine-2-acetic acid lactone (2a, R = CONHPh)**: mp 168.5–169.0 °C (hexane–ethyl acetate); IR (KBr disk) 1760 (s), 1665 (s), 1535 (s), 1445 (s), 1375 (s), 1245 (s), 765 (s), 695 (s) cm^{-1}; ^1H NMR ($CDCl_3$)

δ 2.05 (ddd, J = 4.4, 9.3, 13.9 Hz, 1 H), 2.42 (m, 1 H), 2.78 (dd, J = 2.4, 16.4 Hz, 1 H), 2.92 (dd, J = 4.6, 16.4 Hz, 1 H), 3.44 (ddd, J = 6.1, 9.0, 9.3 Hz, 1 H), 3.67 (ddd, J = 2.4, 4.4, 9.0 Hz, 1 H), 4.64 (dt, J = 2.4, 4.6 Hz, 1 H), 5.06 (t, J = 4.6 Hz, 1 H), 6.43 (br s, 1 H), 7.4 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 30.9, 36.1, 44.2, 58.3, 82.5, 153.5, 175.1. Anal. Calcd for $C_{13}H_{14}N_2O_3$: C, 63.40; H, 5.73; N, 11.38. Found: C, 63.13; H, 5.63; N, 11.24.

***trans*-*N*-(Tolylsulfonyl)-2-[(methoxycarbonyl)methyl]-3-(benzoyloxy)pyrrolidine (benzoate of 3a, R = SO_2Tol)**: mp 149.5–150.0 °C (benzene–hexane); IR (KBr disk) 1745 (s), 1720 (s), 1345 (m), 1165 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz), δ 2.05 (dd, J = 14.0, 6.2 Hz, 1 H), 2.24 (dddd, J = 14.0, 11.8, 8.1, 3.5 Hz, 1 H), 2.31 (s, 3 H), 2.59 (dd, J = 15.8, 10.3 Hz, 1 H), 3.11 (dd, J = 15.8, 4.1 Hz, 1 H), 3.25 (ddd, J = 11.8, 9.2, 6.2 Hz, 1 H), 3.71 (dd, J = 9.2, 8.1 Hz, 1 H), 3.75 (s, 3 H), 4.08 (dd, J = 10.3, 4.1 Hz, 1 H, H_2), 5.26 (d, J = 3.5 Hz, 1 H, H_3); significant NOE is observed on H_2 and one of CH_2CO_2Me protons by irradiation on at H_3; ^{13}C NMR ($CDCl_3$) δ 21.3, 29.7, 39.9, 47.1, 51.7, 62.6, 78.0, 165.0, 170.4. Anal. Calcd for $C_{21}H_{23}NO_6S$: C, 60.42; H, 5.55; N, 3.36; S, 7.68. Found: C, 60.16; H, 5.28; N, 3.09; S, 7.59.

***N*-(Methoxycarbonyl)-5-chloro-3-pentenylamine (7a, R = CO_2Me)**: IR (neat film) 1700 (s), 1530 (s), 1440 (m), 1250 (s), 970 (m), 780 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.25 (m, 2 H), 3.20 (dd, J = 12.0, 6.0 Hz, 2 H), 3.60 (s, 3 H), 3.90 (m, 2 H), 5.60 (m, 2 H).

***N*-(Tolylsulfonyl)-5-chloro-3-pentenylamine (7a, R = SO_2Tol)**: mp 41.5–42.0 °C (benzene–hexane–ether); IR (KBr disk) 3280 (s), 1595 (m), 1430 (m), 1320 (s), 1150 (s), 1090 (s), 965 (m), 815 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.9–2.4 (m, 2 H), 2.43 (s, 3 H), 3.02 (q, J = 6.3 Hz, 2 H), 3.96 (br d, J = 4.4 Hz, 2 H), 4.66 (br t, J = 6.3 Hz, 1 H), 5.4 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 21.2, 31.9, 42.2, 44.2, 126.9, 128.9, 129.5, 130.7, 137.3, 143.2. Anal. Calcd for $C_{12}H_{16}NO_2SCl$: C, 52.75; H, 5.91; N, 5.30. Found: C, 52.64; H, 5.89; N, 5.12.

***cis*-*N*-(Methoxycarbonyl)-3-hydroxy-4,4-dimethylpyrrolidine-2-acetic acid lactone (2b, R = CO_2Me)**: mp 69.5–71.0 °C (ether–hexane); IR (KBr disk) 1780 (s), 1765 (s), 1700 (s), 1450 (s), 1380 (s), 1190 (m), 1145 (m), 1105 (m), 1050 (m), 1000 (m), 770 (m) cm^{-1}; ^{1}H NMR (toluene-d_8, 105 °C) δ 0.86 (s, 3 H), 1.07 (s, 3 H), 2.38 (dd, J = 18.1, 6.2 Hz, 1 H), 2.75 (d, J = 18.1 Hz, 1 H), 3.07 (d, J = 10.7 Hz, 1 H), 3.36 (d, J = 10.7 Hz, 1 H), 3.65 (s, 3 H), 3.84 (d, J = 4.6 Hz, 1 H), 4.21 (dd, J = 6.2, 4.6 Hz, 1 H); ^{13}C NMR (benzene-d_6, 80 °C) δ 20.1, 24.3 (Me), 36.3 (CH_2CO), 41.3 (C_4), 52.5 (Me), 56.7 (C_5), 58.3 (C_2), 89.6 (C_3), 155.3 (NCO), 174.5 (CO_2); mass spectrum, m/z (relative intensity) 213 (M, 62), 198 (42), 156 (36), 114 (32), 44 (100). Anal. Calcd for $C_{10}H_{15}NO_4$: C, 56.32; H, 7.09; N, 6.57. Found: C, 56.25; H, 7.23; N, 6.45.

***cis*-*N*-[(Methylamino)carbonyl]-3-hydroxy-4,4-dimethylpyrrolidine-2-acetic acid lactone (2b, R = CONHMe)**: mp 166.5–167.0 °C (solidifies during standing in a neat state); IR (KBr disk) 1785 (s), 1630 (s), 1550 (s), 1370 (s), 1245 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.06 (s, 3 H), 1.22 (s, 3 H), 2.79 (d, J = 4.6 Hz, 3 H) 2.82 (d, J = 2.2 Hz, 2 H), 3.17 (s, 2 H), 4.41 (d, J = 4.4 Hz, 1 H), 4.66 (dt, J = 4.4, 2.2 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 19.7, 24.2, 26.8, 36.0, 41.4, 55.8, 57.3, 89.1, 156.6, 175.0; high-resolution mass spectrum calcd for $C_{10}H_{16}N_2O_3$ 212.2480, found m/z (relative intensity) 212.1140 (35), 154 (26), 140 (52), 128 (34), 113 (34), 86 (45), 82 (34), 71 (33), 57 (100).

***cis*-*N*-[(Phenylamino)carbonyl]-3-hydroxy-4,4-dimethylpyrrolidine-2-acetic acid lactone (2b, R = CONHPh)**: mp 144.0–144.5 °C (isopropyl ether–benzene–hexane); IR (KBr disk) 1780 (s), 1665 (s), 1535 (s), 1445 (s), 1370 (s), 755 (s), 690 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.11 (s, 3 H), 1.25 (s, 3 H), 2.77 (dd, J = 4.6, 18.6 Hz, 1 H), 2.95 (dd, J = 2.0, 18.6 Hz, 1 H), 3.32 (s, 2 H), 4.43 (d, J = 4.6 Hz, 1 H), 4.76 (dt, J = 2.0, 4.6 Hz, 1 H), 6.29 (br s, 1 H), 7.16–7.49 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 19.7, 24.2, 36.0, 41.5, 56.0, 67.5, 89.1, 153.6, 175.2. Anal. Calcd for $C_{15}H_{18}N_2O_3$: C, 65.68; H, 6.61; N, 10.21. Found: C, 65.95; H, 6.69; N, 10.26.

(6*R,7*R**)- and (6*S**,7*R**)-3,8,8-Trimethyl-7-hydroxy-1,3-diazabicyclo[4.3.0]nonane-2,4-diones (4b and 5b, R′ = Me).** One of the two diastereomers, whose relative configuration is not determined yet, is obtained in a pure form by repeated recrystallization from hexane–tetrahydrofuran: mp 168.5–169.0 °C; IR (KBr disk) 3400 (s), 1710 (s), 1660 (s), 1470 (s), 1310 (s), 1115 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.07 (s, 3 H), 1.16 (s, 3 H), 2.44 (m, 1 H, coalescing to d, J = 15.9 Hz, by irradiation at 3.60), 2.99 (dd, J = 3.8, 15.9 Hz, 1 H), 3.15 (s, 3 H), 3.27 (d, J = 11.6 Hz, 1 H), 3.51 (d, J = 11.6 Hz, 1 H), 3.58–3.64 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 20.3, 24.7, 27.3, 36.5, 39.3, 55.1, 56.6, 83.7, 152.1, 168.9, (the other isomer) 20.4, 25.9, 31.8, 39.0, 41.1, 54.4, 55.7, 78.1, 151.9, 170.4; high-resolution mass spectrum calcd for $C_{10}H_{16}N_2O_3$ 212.1160, found m/e (relative intensity) 212.1156 (11), 210 (100), 155 (71), 140 (44), 110 (53).

Oxidation of a Mixture of 4b and 5b (R′ = Me) to 5,8,8-Trimethyl-1,3-diazabicyclo[4.3.0]nonane-2,4,7-trione. Into a stirred solution of dry pyridine (0.15 mL, 1.8 mmol) in dry dichloromethane (6 mL) was added CrO_3 (91 mg, 0.91 mmol) portionwise over a 15-min period at room temperature. Into this was added a solution of **4b** and **5b** (32 mg, 0.15 mmol, 1:1 mixture) in dry dichloromethane (1 mL), and the resultant solution was stirred at room temperature for 2 h. After evaporation of the solvent, the mixture was diluted with ethyl acetate, washed with 1 N HCl and aqueous $NaHCO_3$, and dried ($MgSO_4$). Evaporation of the solvent, followed by purification by column chromatography over silica gel (benzene–ethyl acetate, 3:1 v/v), provided 5,8,8-trimethyl-1,3-diazabicyclo[4.3.0]nonane-2,4,7-trione as a crystalline solid: yield, 60%; IR (KBr disk) 1760 (s), 1710 (s), 1665 (s), 1470 (m), 1320 (m), cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.23 (s, 3 H), 1.26 (s, 3 H), 2.50 (dd, J = 13.7, 16.6 Hz, 1 H), 3.05 (dd, J = 4.9, 16.6 Hz, 1 H), 3.19 (s, 3 H), 3.40 (d, J = 11.7 Hz, 1 H), 3.29 (dd, J = 13.7, 4.9 Hz, 1 H), 3.99 (d, J = 11.7 Hz, 1 H). Reduction of this trione with 0.5 equiv of $NaBH_4$ in ethanol at room temperature provided a 71:29 mixture of **4b** and **5b** (R′ = Me).

***cis*,*trans*-*N*-(Tolylsulfonyl)-3-hydroxy-5-phenylpyrrolidine-2-acetic acid lactone (2c)**: mp 162.0–163.0 °C (benzene–hexane); IR (KBr disk) 1775 (s), 1315 (m), 1160 (s), 1145 (s), 1090 (m), 1050 (m), 805 (w), 765 (m), 700 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 60 °C) δ 2.16–2.70 (m, 2 H), 2.32 (s, 3 H), 2.98 (dd, J = 19.2, 7.7 Hz, 1 H), 3.28 (dd, J = 19.2, 4.3 Hz, 1 H), 4.78 (ddd, J = 7.7, 7.1, 4.3 Hz, 1 H, coalescing to d, J = 7.1 Hz, by irradiation at 3.18), 4.96 (t, J = 6.9 Hz, 1 H, coalescing to s, by irradiation at 2.43), 5.18 (ddd, J = 7.1, 6.5, 4.3 Hz, 1 H, coalescing to d, J = 7.1 Hz, by irradiation at 2.43), 6.85–7.26 (m, 9 H); ^{13}C NMR ($CDCl_3$, 60 °C) δ 21.3 (Me), 36.2 (CH_2CO), 41.5 (C_4), 60.0 (C_2), 63.3 (C_5), 80.3 (C_3), 174.7 (CO). Anal. Calcd for $C_{19}H_{19}NO_4S$: C, 63.84;, H, 5.36; N, 3.92. Found: C, 64.15; H, 5.27; N, 3.69.

***cis*,*cis*- and *cis*,*trans*-*N*-(Tolylsulfonyl)-3-hydroxy-4-methylpyrrolidine-2-acetic acid lactones (1:1 mixture of stereoisomers of 2d)**: IR (neat film) 1780 (s), 1340 (s), 1160 (s), 815 (m), cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.60 (d, J = 7.3 Hz, 3 H), 1.04 (d, J = 6.8 Hz, 3 H), 1.69–2.11 (m, 2 H), 2.43 (s, 6 H), 2.79–2.94 (m, 4 H), 2.94–3.78 (m, 4 H), 4.33 (m, 1 H, coalescing to d, J = 5.3 Hz, by irradiation at 2.85), 4.47 (m, 1 H, coalescing to d, J = 4.9 Hz, by irradiation at 2.85), 4.57 (m, 1 H, coalescing to d, J = 5.4 Hz, by irradiation at 2.85), 4.80 (t, J = 4.4 Hz, 1 H); high-resolution mass spectrum calcd for $C_{14}H_{17}NO_4S$ 295.0878, found m/z (relative intensity) 295.0876 (6), 140 (11), 86 (64), 84 (100).

***cis*-*N*-(Tolylsulfonyl)-3-methyl-3-hydroxypyrrolidine-2-acetic acid lactone (2e, R = SO_2Tol)**: mp 94.5–95.5 °C (benzene); IR (KBr disk) 1765 (s), 1335 (s), 1275 (m), 1190 (s), 1155 (s), 1115 (s), 945 (s), 820 (s), 735 (s), 655 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.39 (s, 3 H), 1.67 (dd, J = 13.4, 9.3 Hz, 1 H, coalescing to d, J = 13.4 Hz, by irradiation at 3.50), 2.20 (m, 1 H, coalescing to d, J = 13.4 Hz, by irradiation at 3.50), 2.45 (s, 3 H), 2.93 (d, J = 3.9 Hz, 2 H), 3.41–3.59 (m, 2 H), 4.00 (t, J = 3.9 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 21.3 (Me), 22.8 (Me), 36.6 (C_4, CH_2CO), 46.9 (C_5), 64.1 (C_2), 92.1 (C_3), 174.0 (CO). Anal. Calcd for $C_{14}H_{17}NO_4S$: C, 56.93; H, 5.80; N, 4.74; S, 10.86. Found: C, 56.79; H, 5.91; N, 4.72; S, 10.79.

***cis*-*N*-(Methoxycarbonyl)-3-methyl-3-hydroxypyrrolidine-2-acetic acid lactone (2e, R = CO_2Me)**: IR (neat film) 1780 (s), 1700 (s), 1120 (m), 950 (m), cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.52 (s, 3 H), 1.9–2.4 (m, 2 H), 2.84 (d, J = 3.7 Hz, 2 H), 3.17–3.56 (m, 2 H), 3.71 (s, 3 H), 4.10 (t, J = 3.7 Hz, 1 H); high-resolution mass spectrum calcd for $C_9H_{13}NO_4$ 199.0845, found m/z (relative intensity) 199.0854 (29), 171 (60), 156 (49), 128 (100).

***cis*-*N*-[(Methylamino)carbonyl]-3-methyl-3-hydroxypyrrolidine-2-acetic acid lactone (2e, R = CONHMe)**: mp 164.5–165.0 °C (hexane–tetrahydrofuran); IR (KBr disk) 1775 (s), 1640 (s), 1535 (s), 1365 (s), 1230 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.53

(s, 3 H), 2.02 (dd, J = 9.0, 13.7 Hz, 1 H), 2.37 (ddd, J = 2.4, 5.6, 13.7 Hz, 1 H), 2.79 (d, J = 4.6 Hz, 3 H), 2.87 (d, J = 3.4 Hz, 2 H), 3.08–3.77 (m, 2 H), 4.23 (t, J = 3.4 Hz, 1 H), 4.58 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 22.4, 26.8, 35.9, 36.4, 44.1, 62.2, 91.3, 156.5, 174.7. Anal. Calcd for $C_9H_{14}N_2O_3$: C, 54.53; H, 7.12; N, 14.13. Found: C, 54.54; H, 7.27; N, 14.27.

***cis*-*N*-[(Phenylamino)carbonyl]-3-methyl-3-hydroxypyrrolidine-2-acetic acid lactone (2e, R = CONHPh)**: mp 181.5–182.0 °C (hexane–chloroform–benzene); IR (KBr disk) 1760 (s), 1655 (s), 1545 (s), 1445 (s), 1370 (s), 755 (s), 690 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.53 (s, 3 H), 2.04 (dd, J = 9.5, 13.9 Hz, 1 H), 2.35 (dd, J = 5.6, 13.9 Hz, 1 H), 2.89 (d, J = 3.4 Hz, 2 H), 3.55 (m, 1 H), 3.68 (m, 1 H), 4.28 (t, J = 3.4 Hz, 1 H), 6.39 (br s, 1 H), 6.92–7.47 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 22.5, 35.9, 36.5, 44.6, 62.6, 91.2, 153.4, 174.7. Anal. Calcd for $C_{14}H_{16}N_2O_3$: C, 64.60; H, 6.20; N, 10.76. Found: C, 64.60; H, 6.13; N, 10.74.

***N*-(Tolylsulfonyl)-4-methyl-1,2,5,6-tetrahydropyridine (6e, R = SO_2Tol)**: mp 134.0–135.0 °C (benzene–hexane); IR (KBr disk) 1340 (s), 1160 (s), 1095 (m), 955 (m), 820 (m), 740 (m), 670 (m), cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.65 (br s, 3 H), 2.10 (m, 2 H), 2.43 (s, 3 H), 3.16 (t, J = 5.8 Hz, 2 H), 3.52 (m, 2 H), 5.29 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 21.2, 22.6, 30.0, 42.7, 44.6, 116.7, 127.6, 129.4, 134.4, 143.1. Anal. Calcd for $C_{13}H_{17}NO_2S$: C, 62.12; H, 6.82; N, 5.57; S, 12.76. Found: C, 16.59; H, 6.75; N, 5.58; S, 12.63.

***N*-[(Phenylamino)carbonyl]-4-methyl-1,2,5,6-tetrahydropyridine (6e, R = CONHPh)**: mp 128.5–129.0 °C (benzene–hexane); IR (KBr disk) 3330 (s), 1640 (s), 1600 (s), 1540 (s), 1445 (s), 1245 (s), 750 (s), 690 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.74 (br s, 3 H), 2.11 (m, 2 H), 3.58 (t, J = 5.6 Hz, 2 H), 3.90 (m, 2 H), 5.36 (m, 1 H), 6.42 (br s, 1 H), 6.87–7.59 (m, 5 H).

***cis*-*N*-(Methoxycarbonyl)-2-methyl-3-hydroxypyrrolidine-2-acetic acid lactone (2f, R = CO_2Me)**: IR (neat film) 1780 (s), 1690 (s), 1120 (m), 1080 (m), cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.53 (s, 3 H), 2.02–2.26 (m, 2 H), 2.37 (d, J = 19.0 Hz, 1 H), 2.57 (d, J = 19.0 Hz, 1 H), 3.19–3.85 (m, 2 H), 3.70 (s, 3 H), 4.64 (dd, J = 3.2, 1.7 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 60 °C) δ 21.5 (Me), 27.5 (C_4), 40.2 (CH_2CO), 45.4 (C_5), 52.0 (Me), 66.6 (C_2), 88.7 (C_3), 154.2 (CON), 174.4 (CO); high-resolution mass spectrum calcd for $C_9H_{13}NO_4$ 199.0845, found m/z (relative intensity) 199.0852 (24), 157 (100).

***cis*-*N*-[(Phenylamino)carbonyl]-2-methyl-3-hydroxypyrrolidine-2-acetic acid lactone (2f, R = CONHPh)**: mp 152.0–153.0 °C (hexane–chloroform); IR (KBr disk) 1770 (s), 1635 (s), 1530 (s), 1450 (s), 1370 (s), 755 (s), 690 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.60 (s, 3 H), 2.04–2.39 (m, 2 H), 2.60 (d, J = 18.6 Hz, 1 H), 3.59 (d, J = 18.6 Hz, 1 H), 3.34–3.74 (m, 2 H), 4.63 (dd, J = 2.0, 3.2 Hz, 1 H), 6.39 (br s, 1 H), 6.87–7.43 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 21.5, 27.7, 40.2, 44.6, 67.6, 88.2, 152.9, 175.1. Anal. Calcd for $C_{14}H_{16}N_2O_3$: C, 64.60; H, 6.20; N, 10.76. Found: C, 64.43; H, 6.21; N, 10.67.

***cis*-*N*-[(Methylamino)carbonyl]-2-methyl-3-hydroxypyrrolidine-2-acetic acid lactone (2f, R = CONHMe)**: mp 160.0–160.5 °C (hexane–tetrahydrofuran); IR (KBr disk) 1765 (s), 1640 (s), 1550 (s), 1370 (s), 1230 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.59 (s, 3 H), 2.01–2.36 (m, 2 H), 2.62 (d, J = 18.6 Hz, 1 H), 2.78 (d, J = 4.6 Hz, 3 H), 3.15–3.34 (m, 2 H), 3.55 (d, J = 18.6 Hz, 1 H), 4.31 (br s, 1 H), 4.62 (dd, J = 1.7, 3.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 22.0, 26.8, 27.9, 40.4, 44.4, 67.3, 88.4, 156.2, 175.1; high-resolution mass spectrum calcd for $C_9H_{14}N_2O_3$ 198.1004, found m/z (relative intensity) 198.1001 (46), 156 (13), 141 (24), 99 (100).

(6*S,7*R**)-3,6-Dimethyl-7-(benzoyloxy)-1,3-diazabicyclo[4.3.0]nonane-2,4-diones (benzoate of 5f, R′ = Me)**: mp 118.0–118.5 (hexane–tetrahydrofuran); IR (KBr disk) 1775 (s), 1715 (s), 1675 (s), 1450 (s), 1275 (s), 1120 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.29 (s, 3 H), 2.14 (dq, J = 13.1, 9.8 Hz, 1 H), 2.57 (ddt, J = 13.1, 3.3, 8.1 Hz, 1 H), 2.74 (d, J = 16.1 Hz, 1 H), 2.92 (d, J = 16.1 Hz, 1 H), 3.19 (s, 3 H), 3.67 (ddd, J = 11.6, 9.0, 8.2 Hz, 1 H), 3.71 (ddd, J = 11.6, 10.0, 2.3 Hz, 1 H), 5.25 (dd, J = 9.8, 7.4 Hz, 1 H), 7.48 (t, J = 7.5 Hz, 2 H), 7.62 (t, J = 7.5 Hz, 1 H), 8.03 (d, J = 7.1 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 18.6, 26.8, 27.0, 41.6, 43.9, 58.3, 79.3, 151.5, 165.5, 168.2. Anal. Calcd for $C_{16}H_{18}N_2O_4$: C, 63.57; H, 6.00; N, 9.27. Found: C, 63.68; H, 6.21; N, 9.15.

3-Methyl-4-[1(*E*)-propenyl]-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (8g, R′ = Me): IR (neat film) 3300 (s), 1660 (s), 1515 (s), 1450 (s), 970 (m), cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.66–2.25 (m, 2 H), 1.72 (d, J = 5.6 Hz, 1 H), 2.88 (s, 3 H), 3.05–3.54 (m, 2 H), 3.83 (m, 1 H), 5.37 (dd, J = 15.1, 5.4 Hz, 1 H), 5.58 (dq, J = 15.1, 5.6 Hz, 1 H), 5.58 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 16.9, 27.7, 33.1, 36.8, 58.5, 127.2, 130.0, 156.8; mass spectrum, m/z (relative intensity) 154 (M, 49), 139 (57), 113 (100), 84 (72).

3-Phenyl-4-[1(*E*)-propenyl]-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (8g, R′ = Ph): mp 176.0–176.5 °C (benzene–hexane); IR (KBr disk) 3220 (m), 1660 (s), 1495 (s), 1330 (m), 1185 (m), 965 (m), 760 (m), 695 (m); ^{1}H NMR ($CDCl_3$) δ 1.68 (d, J = 5.1 Hz, 3 H), 1.72–2.43 (m, 2 H), 3.14–3.62 (m, 2 H), 4.32 (m, 1 H), 5.39 (br s, 1 H), 5.48 (dd, J = 14.9, 4.2 Hz, 1 H), 5.61 (dq, J = 14.9, 5.1 Hz, 1 H), 7.27 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 17.1, 28.0, 37.3, 59.7, 125.2, 126.6, 127.7, 128.3, 130.0, 143.1, 155.3; mass spectrum, m/z (relative intensity) 216 (M, 60), 201 (51), 146 (36), 119 (100).

***cis*-*N*-[(Phenylamino)carbonyl]-3-hydroxypiperidine-2-acetic acid lactone (10a, R = CONHPh)**: mp 165.0–165.5 °C (benzene–hexane); IR (KBr disk) 1785 (s), 1630 (s), 1535 (m), 1450 (m), 1350 (m), 760 (m), 690 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.57–2.08 (m, 4 H), 2.60 (dd, J = 7.1, 17.8 Hz, 1 H), 2.87 (dd, J = 7.6, 17.8 Hz, 1 H), 3.08–3.74 (m, 2 H), 4.73 (m, 1 H, coalescing to d, J = 7.3 Hz, by irradiation at 1.88), 4.93 (q, J = 7.3 Hz, 1 H), 6.43 (br s, 1 H), 6.86–7.47 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 19.2, 25.6, 33.1, 41.1, 50.2, 75.8, 155.8, 174.5. Anal. Calcd for $C_{14}H_{16}N_2O_3$: C, 64.60; H, 6.20; N, 10.76. Found: C, 64.70; H, 6.08; N, 10.67.

***cis*-*N*-[(Methylamino)carbonyl]-3-hydroxypiperidine-2-acetic acid lactone (10a, R = CONHMe)**: mp 161.5–162.0 °C (hexane–chloroform); IR (KBr disk) 1780 (s), 1625 (s), 1550 (m), 1165 (m), 1030 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.60–1.69 (m, 1 H), 1.75–1.87 (m, 2 H), 1.92–2.01 (m, 1 H), 2.58 (dd, J = 17.8, 7.7 Hz, 1 H), 2.82 (dd, J = 17.8, 8.3 Hz, 1 H), 2.82 (d, J = 4.6 Hz, 3 H), 3.10 (ddd, J = 12.1, 8.1, 4.3 Hz, 1 H), 3.41 (dt, J = 12.1, 6.0 Hz, 1 H), 4.69 (td, J = 6.8, 4.8 Hz, H_3), 4.93 (br q, J = 7.8 Hz, H_2); ^{13}C NMR ($CDCl_3$) δ 19.3, 25.8, 27.5, 32.7, 40.3, 49.9, 75.8, 158.7, 174.7. Anal. Calcd for $C_9H_{14}N_2O_3$: C, 54.53; H, 7.12; N, 14.13. Found: C, 54.25; H, 7.12; N, 13.98.

(6*S,7*R**)-3-Methyl-7-hydroxy-1,3-diazabicyclo[4.4.0]decane-2,4-dione (12a, R′ = Me)**: IR (neat film) 3420 (s), 1715 (s), 1660 (s), 1470 (s), 1285 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.47 (tdd, J = 13.2, 10.8, 4.0 Hz, H_{8a}), 1.62 (tddd, J = 13.2, 12.1, 4.4, 3.3 Hz, H_{9a}), 1.81 (dm, J = 13.2 Hz, H_{9e}), 2.14 (dm, J = 13.2 Hz, H_{8e}), 2.69 (td, J = 12.1, 3.2 Hz, H_{10a}), 2.82 (dd, J = 17.1, 7.2 Hz, H_{5a}), 3.05 (dd, J = 17.1, 6.1 Hz, H_{5e}), 3.14 (ddd, J = 9.4, 7.2, 6.1 Hz, H_6) 3.19 (s, 3 H), 3.38 (ddd, J = 10.8, 9.4, 4.5 Hz, H_7), 4.35 (dm, J = 12.1 Hz, H_{10a}); irradiation of the H_7 proton caused increases of area intensities of H_{5a}, H_{9a}, and H_{8e} protons; ^{13}C NMR ($CDCl_3$) δ 22.9, 27.5, 33.2, 33.5, 45.0, 56.6, 70.9, 153.7, 168.2; high-resolution mass spectrum calcd for $C_9H_{14}N_2O_3$ 198.2212, found m/z (relative intensity) 198.1006 (42), 141 (100), 84 (89), 70 (57).

***N*-(Tolylsulfonyl)-2-vinylpyrrolidine (13a, R = SO_2Tol)**: mp 65.0–66.0 °C (benzene–hexane); IR (KBr disk) 1340 (s), 1155 (s), 1090 (s), 1000 (s), 820 (s), 660 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.71 (m, 4 H), 2.42 (s, 3 H), 3.34 (m, 2 H), 4.17 (m, 1 H), 5.03–5.31 (m, 2 H), 5.82 (ddd, J = 16.8, 9.8, 5.6 Hz, 1 H); mass spectrum, m/e (relative intensity) 251 (M, 27), 224 (60), 187 (58), 186 (58), 155 (49), 96 (100). Anal. Calcd for $C_{13}H_{17}NO_2S$: C, 62.12; H, 6.82; N, 5.57. Found: C, 62.09; H, 6.88; N, 5.74.

***N*-(Methoxycarbonyl)-2-vinylpyrrolidine (13a, R = CO_2Me)**: IR (neat film) 1705 (s), 1455 (s), 1385 (s), 1120 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.60–2.16 (m, 4 H), 3.49 (m, 2 H), 3.68 (s, 3 H), 4.34 (m, 1 H), 4.98–5.30 (m, 2 H), 5.73 (ddd, J = 5.4, 9.8, 17.3 Hz, 1 H); mass spectrum, m/z (relative intensity) 155 (M, 38), 140 (36), 128 (51), 83 (100).

***cis,trans*-*N*-(Methoxycarbonyl)-3-hydroxy-5-methylpiperidine-2-acetic acid lactones (10b)**: IR (neat film) 3360 (s), 1775 (s), 1630 (s), 1540 (s), 1330 (s), cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.03 (d, J = 6.3 Hz, 3 H), 1.42 (ddd, J = 14.9, 11.5, 3.4 Hz, H_{4a}, coalescing to dd, J = 14.9, 11.5 Hz, by irradiation at 4.75), 1.88–2.24 (m, H_{4e} and H_{5a}), 2.4–3.1 (m, CH_2CO and C_{6a}), 2.80 (d, J = 4.6 Hz, 3 H), 3.34 (ddd, J = 11.2, 4.9, 1.5 Hz, H_{6e}, coalescing to d, J = 11.2 Hz, by irradiation at 2.06), 4.55–4.95 (m, H_{2a}, H_{3e}, and NH); ^{13}C NMR ($CDCl_3$) δ 18.9, 23.9, 27.5, 33.5, 36.2, 49.3, 49.8, 76.7, 159.5, 175.2; high-resolution mass spectrum calcd for $C_{10}H_{16}N_2O_3$ 212.1160, found m/z (relative intensity) 212.1146 (32), 155 (100), 113 (77), 96 (46).

***cis*-*N*-[(Methylamino)carbonyl]-3-hydroxy-3,5,5-trimethylpiperidine-2-acetic acid lactone (10c, R = CONHMe)**: IR (neat film) 1770 (s), 1630 (s), 1545 (s), 1260 (s), 1225 (s); ^{1}H NMR ($CDCl_3$) δ 1.03 (s, 6 H), 1.47 (s, 3 H), 1.60 (d, J = 14.6 Hz, 1 H), 1.79 (d, J = 14.6 Hz, 1 H), 2.53 (dd, J = 5.9, 18.3 Hz, 1 H), 2.79 (d, J = 14.4 Hz, 1 H), 2.81 (d, J = 5.1 Hz, 3 H), 2.88 (d, J = 8.1, 18.3 Hz, 1 H), 3.13 (d, J = 14.4 Hz, 1 H), 4.60 (br s, 1 H), 5.69 (dd, J = 5.9, 8.1 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 27.3, 27.4, 28.5, 30.5, 32.9, 45.4, 49.7, 55.3, 83.4, 158.3, 174.2; high-resolution mass spectrum calcd for $C_{12}H_{20}N_2O_3$ 240.1474, found m/z (relative intensity) 240.1477 (9), 183 (32), 168 (30), 124 (36), 97 (21), 57 (100).

***cis*-*N*-[(Phenylamino)carbonyl]-3-hydroxy-3,5,5-trimethylpiperidine-2-acetic acid lactone (10c, R = CONHPh)**: mp 180.5–181.0 °C (hexane–benzene–THF); IR (KBr disk) 1770 (s), 1635 (s), 1535 (s), 1450 (s), 755 (m), 690 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.05 (s, 3 H), 1.09 (s, 3 H), 1.47 (s, 3 H), 1.60 (d, J = 14.9 Hz, 1 H), 1.84 (d, J = 14.9 Hz, 1 H), 2.55 (dd, J = 5.6, 18.3 Hz, 1 H), 2.84 (d, J = 14.2 Hz, 1 H), 2.93 (dd, J = 7.8, 18.3 Hz, 1 H), 3.36 (d, J = 14.2 Hz, 1 H), 4.76 (dd, J = 5.6, 7.8 Hz, 1 H), 6.65 (br s, 1 H), 6.9–7.6 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 27.6, 28.1, 28.6, 30.8, 33.5, 45.3, 50.8, 55.5, 83.7, 155.3, 174.2. Anal. Calcd for $C_{17}H_{22}N_2O_3$: C, 67.53; H, 7.33; N, 9.26. Found: C, 67.52; H, 7.37; N, 9.17.

7-Hydroxy-7,9,9-trimethyl-1,3-diazabicyclo[4.4.0]decane-2,4-dione (a mixture of 11c and 12c, R′ = Me): mp 133.5–134.5 °C (4:1 mixture of diastereomers, ether–hexane); IR (KBr disk) 3480 (s), 1710 (s), 1660 (s), 1480 (s), 1280 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$) major isomer δ 1.00 (s, 3 H), 1.02 (s, 3 H), 1.22 (s, 3 H), 1.35–1.55 (m, 2 H), 1.77 (dd, J = 13.3, 1.7 Hz, H_{5e}), 2.58 (d, J = 13.1, Hz, H_{10a}), 2.77–3.31 (m, 3 H), 3.20 (s, 3 H), 4.24 (dd, J = 13.1, 1.7 Hz, H_{10e}), minor isomer δ 0.94 (s, 3 H), 1.14 (s, 3 H), 1.19 (s, 3 H), 2.53 (d, J = 13.4 Hz, H_{10a}), 3.20 (s, 3 H), 4.29 (dd, J = 13.4, 2.3 Hz, H_{10e}); high-resolution mass spectrum calcd for $C_{12}H_{20}N_2O_3$ 240.1474, found m/z (relative intensity) 240.1481 (6), 183 (64), 181 (51), 141 (100).

***N*-[(Phenylamino)carbonyl]-6-chloro-2,2,4-trimethyl-4-hexenylamine (14c, R = CONHPh)**: IR (neat film) 3340 (s), 1640 (s), 1450 (s), 1320 (s), 1240 (s), 750 (s), 695 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.98 (s, 6 H), 1.62 (br s, 1 H), 1.77 (s, 3 H), 2.13 (s, 2 H), 3.43 (s, 2 H), 3.87 (d, J = 5.6 Hz, 2 H), 5.72 (t, J = 5.6 Hz, 1 H), 6.32 (br s, 1 H), 6.87–7.48 (m, 6 H).

***N*-[(Phenylamino)carbonyl]-6-acetoxy-2,2,4-trimethyl-4-hexenylamine**: IR (neat film) 3350 (s), 1740 (s), 1650 (s), 1600 (s), 1560 (s), 1500 (s), 1235 (s), 750 (m), 690 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.90 (s, 6 H), 1.77 (br s, 3 H), 1.96–2.17 (m, 2 H), 2.07 (s, 3 H), 3.10 (d, J = 6.1 Hz, 2 H), 4.58 (d, J = 6.8 Hz, 2 H), 5.28 (t, J = 6.8 Hz, 2 H), 5.31 (br s, 1 H), 6.82–7.56 (m, 6 H); mass spectrum, m/z (relative intensity) 258 (M – AcOH, 60), 243 (23), 166 (100), 124 (61), 98 (40).

***N*-[(Methylamino)carbonyl]-2-[1(*E*)-propenyl]pyrrolidine (13d)**: IR (neat film) 3340 (s), 1630 (s), 1540 (s), 1370 (s), 1145 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.57–2.27 (m, 4 H), 1.71 (d, J = 5.6 Hz, 3 H), 2.76 (d, J = 4.6 Hz, 3 H), 3.2–3.7 (m, 2 H), 4.10 (m, 1 H), 4.38 (br s, 1 H), 5.39 (dd, J = 5.9, 15.4 Hz, 1 H), 5.62 (dq, J = 15.4, 5.6 Hz, 1 H); mass spectrum, m/z (relative intensity) 168 (M, 8), 96 (38), 84 (100).

Aminomercuriation of 1a, 1f, and 9e. Into a stirred solution of **1a** (R = CO_2Me, 159 mg, 1 mmol) in THF (10 mL) was added mercuric acetate (640 mg, 2 mmol), and the mixture was stirred overnight at room temperature. An excess of $NaBH_4$ (2 mmol) dissolved in ethanol–H_2O was added into this solution. After stirring for 2 h and evaporation of the solvent, the mixture was diluted with ether and washed with saturated NaCl. The organic layer was dried ($MgSO_4$) and condensed to leave an oil, which was purified by column chromatography over silica gel (benzene–ethyl acetate, 1:1 v/v) to give a 91:9 mixture of *cis*- (**19**) and *trans*-*N*-(methoxycarbonyl)-2-methyl-3-hydroxypyrrolidines (**20**) in 85% yield. *N*-(Methoxycarbonyl)-2,2-dimethyl-3-hydroxypyrrolidine was obtained in 86% yield by aminomercuriation of **1f** (R = CO_2Me) upon exposure to mercuric acetate (1.1 equiv) in dimethoxyethane–H_2O (4 mL, 2 mL/mmol of **1f**) overnight, followed by addition of $NaBH_4$ (1.1 equiv). Benzoylation of **19** and inversion of **19** to the benzoate of **20** were carried out according to the procedure reported previously.[1b] Aminomercuriation of **9e** (R = SO_2Tol, CO_2Me, CONHPh) was undertaken under conditions similar to those for **1f** (at ambient temperature for 13 h), and a mixture of **21** and **22**, whose stereochemistry was unknown, was obtained: 45% based on 57% conversion, 63:37 for R = SO_2Tol; 56% based on 95% conversion, 59:41 for R = CO_2Me; 66% based on 95% conversion, 69:31 for R = CONHPh. The starting material was recovered for the aminomercuriation of **9e** (R = SO_2Tol) under conditions similar to those for **1a** (R = CO_2Me).

***cis*-*N*-(Methoxycarbonyl)-2-methyl-3-hydroxypyrrolidine (19)**: IR (neat film) 3400 (s), 1680 (br s), 1455 (s), 1390 (s), 1200 (m), 1130 (m), 1080 (m), 775 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 60 °C) δ 1.20 (d, J = 6.6 Hz, 3 H), 1.97 (m, 2 H), 3.43 (m, 2 H), 3.69 (s, 3 H), 3.93 (quint, J = 6.6 Hz, 1 H), 4.32 (m, 1 H); ^{13}C NMR ($CDCl_3$, 60 °C) δ 13.1 (Me), 30.6 (C_4), 43.0 (C_5), 51.8 (Me), 55.8 (C_2), 71.4 (C_3), 155.5 (CO).

***cis*-*N*-(Methoxycarbonyl)-2-methyl-3-(benzoyloxy)-pyrrolidine (benzoate of 19)**: mp 124.0–124.5 °C (hexane); IR (KBr disk) 1715 (s), 1685 (s), 1445 (s), 1380 (s), 1270 (s), 1110 (br s), 1020 (m), 770 (m), 710 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 60 °C) δ 1.26 (d, J = 6.4 Hz, 3 H), 2.17 (m, 2 H), 3.55 (m, 2 H), 3.72 (s, 3 H), 4.23 (quint, J = 6.4 Hz, 1 H), 5.46 (q, J = 6.4 Hz, coalescing to d, J = 6.4 Hz, by irradiation at 2.17, 1 H), 7.3–7.6 (m, 3 H), 8.0–8.1 (m, 2 H); ^{13}C NMR ($CDCl_3$, 60 °C) δ 14.3 (Me), 28.9 (C_4), 43.3 (C_5), 52.0 (Me), 59.4 (C_2), 72.3 (C_3), 155.4 (CON), 165.6 (CO_2). Anal. Calcd for $C_{14}H_{17}NO_4$: C, 63.86; H, 6.51; N, 5.31. Found: C, 63.81; H, 6.50; N, 5.44.

***trans*-*N*-(Methoxycarbonyl)-2-methyl-3-(benzoyloxy)-pyrrolidine (benzoate of 20)**: mp 118.5–119.0 °C (hexane); IR (KBr disk) 1700 (s), 1680 (s), 1445 (m), 1380 (m), 1280 (br s), 1115 (m), 940 (br m), 770 (m), 700 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 60 °C) δ 1.28 (d, J = 6.7 Hz, 3 H), 1.96–2.52 (m, 2 H), 3.50–3.70 (m, 2 H), 3.72 (s, 3 H), 4.09 (q, J = 6.7 Hz, coalescing to s, by irradiation at 1.28, 1 H), 5.17 (dd, J = 1.7, 3.9 Hz, 1 H), 7.3–7.6 (m, 3 H), 8.0–8.1 (m, 2 H); ^{13}C NMR ($CDCl_3$, 60 °C) δ 18.0 (Me), 28.8 (C_4), 44.2 (C_5), 52.1 (Me), 59.3 (C_2), 79.4 (C_3), 155.4 (CON), 165.7 (CO_2). Anal. Calcd for $C_{14}H_{17}NO_4$: C, 63.86; H, 6.51; N, 5.31. Found: C, 64.02; H, 6.41; N, 5.08.

***N*-(Methoxycarbonyl)-2,2-dimethyl-3-hydroxypyrrolidine**: bp 135 °C (0.08 mmHg); IR (neat film) 3430 (s), 1675 (br s), 1445 (s), 1380 (s), 1090 (s), 775 (m); ^{1}H NMR ($CDCl_3$, 60 °C) δ 1.34 (s, 3 H), 1.36 (s, 3 H), 1.71 (d, J = 5.4 Hz, OH), 1.62–2.26 (m, 2 H), 3.25–3.60 (m, 2 H), 3.62 (s, 3 H), 3.87 (q, J = 5.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 60 °C) δ 19.7 (br, Me), 25.3 (br, Me), 29.7 (C_4), 44.1 (C_5), 51.6 (br, Me), 62.7 (C_2), 79.3 (C_3).

***cis*- and *trans*-*N*-[(Phenylamino)carbonyl]-2,3-dimethyl-3-hydroxypiperidine (21 and 22).** These isomers, whose structures are not determined yet, were separated by means of recrystallization from hexane–tetrahydrofuran. One isomer: mp 188.5–189.0 °C (hexane–tetrahydrofuran); IR (KBr disk) 3300 (s), 1625 (s), 1545 (s), 1440 (s), 750 (s), 695 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.20 (s, 3 H), 1.21 (d, J = 7.1 Hz, 3 H), 1.41–2.02 (m, 4 H), 2.51 (br s, 1 H), 3.05 (m, 1 H), 3.91 (dd, J = 3.9, 14.6 Hz, 1 H), 4.05 (q, J = 7.1 Hz, 1 H), 6.60 (br s, 1 H), 6.85–7.43 (m, 5 H). The other isomer: mp 154.0–154.5 °C (hexane–tetrahydrofuran); IR (KBr disk) 3300 (s), 1640 (s), 1540 (s), 1450 (s), 750 (s), 695 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.24 (d, J = 7.1 Hz, 3 H), 1.36 (s, 3 H), 1.44–1.86 (m, 4 H), 1.97 (br s, 1 H), 3.02 (m, 1 H), 3.87 (m, 1 H), 4.02 (q, J = 7.1 Hz, 1 H), 6.56 (br s, 1 H), 6.69–7.48 (m, 5 H). Anal. Calcd for $C_{14}H_{20}N_2O_2$: C, 67.72; H, 8.12; N, 11.28. Found: C, 67.58; H, 8.38; N, 11.13.

***cis*-2,6-Dimethyl-4-benzyl-2,4-diaza-7-oxabicyclo[4.3.0]-nonane-3,8-dione (24)**: mp 130.5–131.5 °C (benzene–hexane); IR (KBr disk) 1770 (s), 1640 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.40 (s, 3 H), 2.67 (dd, J = 4.0, 15.4 Hz, 1 H), 2.80 (dd, J = 7.5, 15.4 Hz, 1 H), 2.86 (s, 3 H), 3.13 (d, J = 13.4 Hz, 1 H), 3.20 (d, J = 13.4 Hz, 1 H), 3.74 (dd, J = 4.0, 7.5 Hz, 1 H), 4.36 (d, J = 14.6 Hz, 1 H), 4.63 (d, J = 14.6 Hz, 1 H), 7.26 (s, 5 H); mass spectrum, m/z (relative intensity) 274 (M, 100), 215 (20), 131 (15), 91 (30). Anal. Calcd for $C_{15}H_{18}N_2O_3$: C, 65.66; H, 6.63; N, 10.21; O, 17.50. Found: C, 65.86; H, 6.63; N, 10.29; O, 17.50.

1-Benzyl-3,4-dimethyl-4-vinyl-2-imidazolidinone (25): IR (neat film) 1695 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.29 (s, 3 H), 2.68 (s, 3 H), 2.92 (d, J = 9.5 Hz, 1 H), 3.04 (d, J = 9.5 Hz, 1 H), 4.38 (s, 2 H), 5.09 (d, J = 16.9 Hz, 1 H), 5.15 (d, J = 10.1 Hz, 1 H), 5.78 (m, 1 H), 7.3 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 20.4, 25.2, 47.9, 55.6, 58.5, 115.4, 127.0, 127.7, 128.4, 137.1, 139.8, 159.9; mass

spectrum, m/z (relative intensity) 230 (M, 30), 215 (45), 91 (100).

Palladium-Catalyzed Decarboxylation of *N*-(*p*-Tolylsulfonyl)-4,4-dimethyl-3-vinyl-2-oxa-6-azacyclohexan-1-one (15). (a) Under a Carbon Monoxide Atmosphere. A mixture of **15** (340 mg, 1 mmol) and $Pd(OAc)_2(PPh_3)_2$ (22.5 mg, 0.03 mmol) in dry ethanol (10 mL) was stirred at ambient temperature for 24 h and then at 60 °C for 30 h in a flask fitted with a reflux condenser equipped at the top with a balloon containing CO. The solvent was removed, and the residue was directly chromatographed over silica gel (benzene–ethyl acetate gradient) to give ethyl *N*-(*p*-tolylsulfonyl)-5,5-dimethyl-6-amino-3-hexenoate (**17**) in 84% yield as an oil: bp 220 °C (1 mmHg); IR (neat film) 3280 (m), 1735 (s), 1330 (s), 1160 (s), 1095 (m), 660 (s), cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00 (s, 6 H), 1.27 (t, J = 7.1 Hz, 3 H), 2.42 (s, 3 H), 2.72 (d, J = 6.6 Hz, 2 H), 2.98 (d, J = 6.1 Hz, 2 H), 4.15 (q, J = 7.1 Hz, 2 H), 4.54 (t, J = 6.1 Hz, 1 H), 5.32 (d, J = 15.9 Hz, 1 H), 5.56 (dt, J = 15.9, 6.1 Hz, 1 H), 7.29 (d, J = 9.0 Hz, 2 H), 7.73 (d, J = 9.0 Hz, 2 H); mass spectrum, m/z (relative intensity) 294 (M – EtO, 28), 250 (5), 185 (M – Ts, 83), 155 (Ts). Anal. Calcd for $C_{17}H_{25}NSO_4$: C, 60.15; H, 7.42; N, 4.13; S, 9.44. Found: C, 60.35; H, 7.48; N, 4.16; S, 9.46.

(b) Under an Argon Atmosphere. A mixture of **15** (340 mg, 1 mmol) and tetrakis(triphenylphosphine)palladium (35 mg, 0.03 mmol) in dry ethanol (20 mL) was stirred under argon at room temperature for 41 h and then at 60 °C for 29 h. The solvent was removed, and the residue was chromatographed over silica gel (benzene–ethyl acetate gradient) to give *N*-(tolylsulfonyl)-3,3-dimethyl-2-vinylazetidine (**18**) in 39% yield: mp 58–60 °C (benzene–hexane); IR (KBr disk) 1340 (s), 1160 (s), 985 (s), 920 (s), 820 (s), 750 (s), 665 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.86 (s, 3 H), 1.11 (s, 3 H), 2.45 (s, 3 H), 3.29 (d, J = 7.3 Hz, 1 H), 3.84 (d, J = 6.8 Hz, 1 H), 5.12–5.40 (m, 2 H), 5.86 (ddd, J = 6.8, 10.0, 17.1 Hz, 1 H), 7.34 (d, J = 8.3 Hz, 2 H), 7.70 (d, J = 8.3 Hz, 2 H). Anal. Calcd for $C_{14}H_{19}NO_2S$: C, 63.37; H, 7.22; N, 4.28; S, 12.08. Found: C, 63.40; H, 7.22; N, 5.11; S, 11.99.

Acknowledgment. We acknowledge partial financial support from the Ministry of Education, Science and Culture, the Japanese Government (Grant-in-Aid for Special Project No. 60 119 002 and 61 125 002, Scientific Research B No. 61 470 094, and Grant-in-Aid for Co-operative Research No. 62 303 003).

Registry No. **1a** (R = SO_2Tol), 90778-63-5; **1a** (R = CO_2Me), 102564-64-7; **1a** (R = CONHPh), 116699-58-2; **1b** (R = CO_2Me), 101926-93-6; **1b** (R = CONHMe), 116699-59-3; **1b** (R = CONHPh), 116699-60-6; **1c**, 101926-94-7; **1d** (isomer 1), 90778-67-9; **1d** (isomer 2), 90778-68-0; **1e** (R = SO_2Tol), 90778-66-8; **1e** (R = CO_2Me), 116699-61-7; **1e** (R = CONHMe), 116699-62-8; **1e** (R = CONHPh), 116699-63-9; **1f** (R = SO_2Tol), 90778-64-6; **1f** (R = CO_2Me), 101926-92-5; **1f** (R = CONHMe), 116699-64-0; **1f** (R = CONHPh), 116699-65-1; **1g** (R = SO_2Tol), 116699-66-2; **1g** (R = CO_2Me), 116699-67-3; **1g** (R = CONHMe), 116699-68-4; **1g** (R = CONHPh), 116699-69-5; **2a** (R = SO_2Tol), 101927-00-8; **2a** (R = CO_2Me), 101926-97-0; **2a** (R = CONHPh), 116699-85-5; **2b** (R = CO_2Me), 101926-98-1; **2b** (R = CONHMe), 116699-87-7; **2b** (R = CONHPh), 116699-90-2; **2c**, 116781-98-7; **2d** (isomer 1), 116781-99-8; **2d** (isomer 2), 116782-00-4; **2e** (R = SO_2Tol), 101927-03-1; **2e** (R = CO_2Me), 116699-91-3; **2e** (R = CONHMe), 116699-92-4; **2e** (R = CONHPh), 116699-93-5; **2f** (R = CO_2Me), 101926-99-2; **2f** (R = CONHMe), 116699-94-6; **2f** (R = CONHPh), 116699-96-8; **3a** (R = SO_2Tol), 116699-82-2; **4b** (R = CONHMe, R′ = Me), 116699-88-8; **5b** (R = CONHMe, R′ = Me), 116699-89-9; **5f** (R′ = Me), 116699-95-7; **7a** (R = SO_2Tol), 116699-83-3; **7a** (R = CO_2Me), 116699-84-4; **7b** (R = CO_2Me), 116699-86-6; **6e** (R = SO_2Tol), 101926-95-8; **6e** (R = CONHPh), 62836-54-8; **8a** (R′ = Me), 116699-97-9; **8a** (R′ = Ph), 116699-98-0; **9a** (R = SO_2Tol), 116699-70-8; **9a** (R = CO_2Me), 116699-71-9; **9a** (R = CONHMe), 116699-72-0; **9a** (R = CONHPh), 116699-73-1; **9b**, 116699-74-2; **9c** (R = CONHMe), 116699-75-3; **9c** (R = CONHPh), 116699-76-4; **9d**, 116699-77-5; **9e** (R = SO_2Tol), 116700-13-1; **9e** (R = CO_2Me), 116700-14-2; **9e** (R = CONHPh), 116700-15-3; **10a** (R = CONHMe), 116700-01-7; **10a** (R = CONHPh), 116700-03-9; **10b**, 116700-04-0; **10c** (R = CONHMe), 116700-06-2; **10c** (R = CONHPh), 116700-10-8; **11b**, 116700-05-1; **11c** (R′ = Me), 116700-07-3; **12ia** (R′ = Me), 116700-02-8; **12c** (R′ = Me), 116700-08-4; **13a** (R = SO_2Tol), 116699-99-1; **13a** (R = CO_2Me), 84193-80-6; **13d**, 116700-12-0; **14c** (R = CONHMe), 116700-09-5; **14c** (R = CONHPh), 116724-48-2; **15**, 116700-29-9; **17**, 116700-30-2; **18**, 116700-31-3; **19**, 116700-16-4; **20**, 116700-17-5; **21** (R = SO_2Tol), 116700-21-1; **21** (R = CO_2Me), 116700-23-3; **21** (R = CONHPh), 116700-25-5; **22** (R = SO_2Tol), 116700-22-2; **22** (R = CO_2Me), 116700-24-4; **22** (R = CONHPh), 116700-26-6; **23** (X = NCH_2Ph), 116699-80-0; **23** (X = O), 116699-81-1; **24**, 116700-27-7; **25**, 116700-28-8; $PdCl_2$, 7647-10-1; *N*,*N*-dimethylacetamide, 127-19-5; 3-iodopropionitrile, 2517-76-2; crotonoyl chloride, 10487-71-5; *trans*-4-oxo-5-heptenenitrile, 116699-78-6; *N*-hydroxy-4-oxo-5-heptenylamine, 116699-79-7; 2-methyl-1,3-butadiene 1,2-epoxide, 1838-94-4; *N*-(methoxycarbonyl)-6-acetoxy-4-hexenylamine, 116700-00-6; *N*-[(phenylamino)carbonyl]-2,2,4-trimethyl-6-acetoxy-4-hexenylamine, 116700-11-9; *N*-(methoxycarbonyl)-2,2-dimethyl-3-hydroxypyrrolidine, 116700-18-6; *cis*-*N*-(methoxycarbonyl)-2-methyl-3-(benzoyloxy)pyrrolidine, 116700-19-7; *trans*-*N*-(methoxycarbonyl)-2-methyl-3-(benzoyloxy)pyrrolidine, 116700-20-0; 5,5,8-trimethyl-1,3-diazabicyclo[4.3.0]nonane-2,4,7-trione, 116724-49-3.