# Palladium(II)-Catalyzed Intramolecular Aminocarbonylation of *endo*-Carbamates under Wacker-Type Conditions

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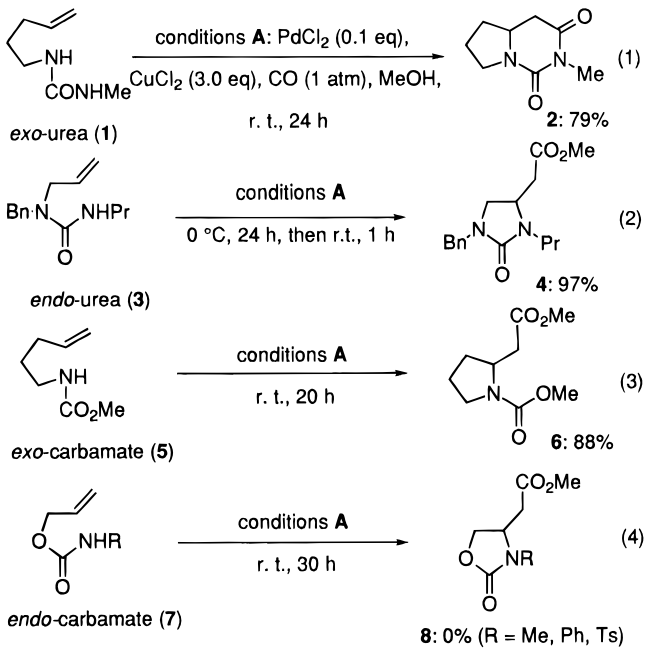
Pd(II)-catalyzed intramolecular aminocarbonylation of olefins bearing many types of nitrogen nucleophiles has been examined under two typical conditions: acidic conditions [conditions A, typically $PdCl_2$ (0.1 equiv) and $CuCl_2$ (3.0 equiv) under 1 atm of CO at room temperature in methanol] and buffered conditions [conditions B, typically $PdCl_2$ (0.1 equiv) and $CuCl_2$ (2.3 equiv) under 1 atm of CO at 30 °C in trimethyl orthoacetate]. Among nitrogen nucleophiles, *endo*-carbamates **7** display distinctive reactivity: *endo*-carbamates **7a**−**k** smoothly undergo intramolecular aminocarbonylation under conditions B to furnish 4-[(methoxycarbonyl)methyl]-2-oxazolidinones **8a**−**k** in good yields, while they would not undergo the expected reaction under conditions A. Other nitrogen nucleophiles (*exo*-ureas **1**, *endo*-ureas **3**, *exo*-carbamates **5**, and *exo*-tosylamides **9**), on the other hand, satisfactorily undergo aminocarbonylation only under conditions A to give rise to **2**, **4**, **6**, and **10**, respectively, in good yields. Under conditions B, they are unreactive and provide either the expected products in poor yields or intractable mixtures of products. On the basis of this contrasting reactivity between *endo*-carbamates and other nitrogen nucleophiles, the chemoselective aminocarbonylation of **7l**−**o** has been achieved; aminocarbonylation takes place at the *endo*-carbamate moieties to furnish **8l**−**o** exclusively under conditions B, and aminocarbonylation occurs at the *exo*-carbamate, *exo*-urea, and *exo*-tosylamide moieties to yield **13a**−**d** exclusively under conditions A.

## Introduction

Despite its importance as an efficient and straightforward method for preparation of physiologically valuable $\beta$-amino acid derivatives, the transition-metal-catalyzed aminocarbonylation of olefins has not been intensively studied.[1]

We have demonstrated that nitrogen nucleophiles, depending on the structure type, display completely different reaction behavior in the Wacker-type intramolecular aminocarbonylation (eqs 1−4). For example, ureas **1** and **3**[2,3] and carbamate **5**[3] smoothly undergo intramolecular aminocarbonylation under the Wacker-type conditions utilizing palladium(II) chloride as a catalyst and copper(II) chloride as an oxidant under 1 atm of carbon monoxide in methanol at an ambient temperature or below (eqs 1−3, conditions A, Table 1). Carbamates **7** (R = Me, Ph, Ts), on the other hand, do not undergo aminocarbonylation under similar conditions:[2] They either are unreactive or provide intractable mixtures of products.

In order to conveniently differentiate the structure type of these substrates, carbamates **5** and **7** are referred to as *exo*- and *endo*-carbamates, respectively. *exo*-Carbamates are those that, on cyclization, provide nitrogen heterocycles possessing a carbamate functionality as a ring substituent. *endo*-Carbamates are those giving rise to nitrogen heterocycles containing a carbamate moiety as a ring constituent. In a similar way, ureas **1** and **3** may be termed as *exo*- and *endo*-ureas, respectively.




As is apparent from the reaction temperatures and times shown in eqs 1 and 2, *endo*-ureas are, in general, more reactive than *exo*-ureas. In view of the relative reactivity between *endo*- and *exo*-ureas, the exceedingly low reactivity of *endo*-carbamates (eq 4), as compared with *exo*-carbamates (eq 3), has long been a question to be addressed.[4]

We report here that the aminocarbonylation of *endo*-carbamates **7** is greatly facilitated by a slight modifica-

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(1) Hegedus, L. S. *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I.; Semmelhack, M. F., Eds.; Pergamon Press: Oxford, U.K., 1991; Vol. 4, pp 559−563.
(2) Tamaru, Y.; Hojo, M.; Higashimura, H.; Yoshida, Z. *J. Am. Chem. Soc.* **1988**, *110*, 3994−4002. See also, Bäckvall, J.-E.; Andersson, P. G. *J. Am. Chem. Soc.* **1990**, *112*, 3683−3685.
(3) Tamaru, Y.; Hojo, M.; Yoshida, Z. *J. Org. Chem.* **1988**, *53*, 5731−5741.

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**Table 1. Typical Reaction Conditions for the Intramolecular Aminocarbonylation of *endo*-Carbamates 7 and 11[a]**

| conditions | $PdCl_2$ (mmol) | $CuCl_2$ (mmol) | base (3 mmol) | additive (18 mmol) | solvent (mL) |
|---|---|---|---|---|---|
| A | 0.10 | 3.0 | none | none | MeOH (5) |
| B-1 | 0.25 | 2.3 | AcONa | AcOH[b] | MeOH (2) |
| B-2 | 0.25 | 2.3 | AcONa | MOA | MeOH (8) |
| B-2′ | 0.10 | 2.3 | AcONa | MOA | MeOH (8) |
| B-3 | 0.10 | 2.3 | none | none | MOA (5) |
| B-3′ | 0.05 | 2.3 | none | none | MOA (5) |

[a] **7** or **11** (1 mmol) under 1 atm of CO. [b] 5 mL.

tion of conditions A, namely, by using sodium acetate (3 equiv) in combination with either acetic acid (5 mL, conditions B-1, Table 1) or trimethyl orthoacetate (MOA) (18 equiv, conditions B-2, Table 1). Furthermore, the reaction of **7** nicely proceeds by using MOA as a solvent (conditions B-3 or B-3′, Table 1). Significantly, conditions B-3 and A, the former being effective for aminocarbonylation of *endo*-carbamates **7** and the latter for that of the other nitrogen nucleophiles **1**, **3**, **5**, differ only in the solvents used. Conditions B can be successfully applied to the reaction of *endo*-carbamates **11**, one-carbon higher homologues of **7** (eqs 8 and 9).

Under conditions B, all the *exo*-nitrogen nucleophiles (**1**, **3**, **5**, and **9**) react very slowly, providing the expected cyclization products, albeit in low yields, if any. Accordingly, the chemoselective aminocarbonylation of **7l**−**o** at the *endo*-carbamate moieties to provide **8l**−**o** (under conditions B) and at the other nitrogen nucleophiles to furnish **13a**−**d** (under conditions A) has been achieved with perfect selectivity (Scheme 2). This paper is a full account of our preliminary communications.[5]

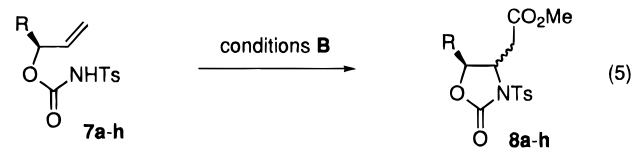
## Results and Discussion

**Aminocarbonylation of 2-Propenyl Carbamates 7.** We have demonstrated previously that a wide variety of *exo*-carbamates, e.g., **5**, smoothly undergo intramolecular aminocarbonylation to provide 2-[(methoxycarbonyl)methyl]pyrrolidines in excellent yields under conditions A (eq 3).[3] *endo*-Carbamates **7**, on the other hand, would not undergo the expected aminocarbonylation at all under similar or somewhat forcing conditions. For example, the reaction of **7e** (run 1, Table 2) was very sluggish and provided a very complex mixture of products after prolonged reaction time at elevated temperature. Despite careful examination of the reaction mixture by TLC and $^1H$ NMR, the expected aminocarbonylation product **8e** was not detected at all. During examination of the reaction conditions, we noticed that MOA (run 2, Table 2) and sodium acetate (run 3) were effective in promoting the reaction. A drawback to these reactions, however, was the complexity of the obtained products. In any event, with 18 equiv of MOA (run 2, Table 2), we, for the first time, succeeded in the isolation of the expected product **8e** in 45% yield by careful purification of the reaction mixture by flash column chromatography over silica gel.

With 3 equiv of sodium acetate (run 3, Table 2), the reaction ceased essentially at ca. 50% conversion owing to precipitation of palladium black. From the reaction mixture, **8e** was isolated in 43% yield (based on 48% conversion). We took the precipitation of palladium black as the result of abuse of $CuCl_2$ for some $PdCl_2$-mediated side reactions under such basic conditions, e.g., oxidation of methanol to formaldehyde and oxidation of carbon monoxide to dimethyl carbonate.[6]

In order to suppress such side reactions, we applied a sodium acetate−acetic acid buffer (conditions B-1, run 4 in Table 2). Eventually, conditions B-1 turned out to be successful for the reaction of a limited number of *endo*-carbamates (e.g., **7a**−**c**, Table 3); however, the conditions were still not acceptable for the aminocarbonylation of **7e**, providing **8e**, albeit in a low yield, after an unreasonably long reaction time. Finally, we found that the combination of sodium acetate (3 equiv) and MOA (18 equiv) greatly accelerated the reaction and improved the yield (conditions B-2, run 5 in Table 2). The reaction was clean, and the spectroscopically homogeneous **8e** was obtained in a quantitative yield just by extraction of the reaction mixture.

Aminocarbonylation of a variety of *endo*-carbamates **7a**−**h** was examined under the thus optimized conditions B-1 and B-2 (eq 5). Results are summarized in Table 3,




(5)

where analogs **7** are arranged in the order of approximate increases in the steric bulkiness of the C-1 substituents. From this table, it is apparent that (1) conditions B-1 are only acceptable for the reactions of **7a**−**d** bearing the sterically small substituents on C-1; (2) for all the analogs of **7** examined, conditions B-2 bring about better yields within much shorter reaction times; (3) *trans*-**8** are obtained with higher stereoselectivities under conditions B-1 than under conditions B-2; and (4) the amount of $PdCl_2$ may be reduced from 0.25 equiv (conditions B-2) to 0.10 equiv (conditions B-2′) without serious deterioration in the yields (runs 12 and 16, Table 3).

Even under the thus optimized conditions B-2, palladium black still precipitated in the reactions of some *endo*-carbamates **7f**−**h**, especially those bearing the sterically bulky C-1 substituents (runs 19, 21, and 23 in Table 3). In an attempt to improve the conversions and yields, we examined the aminocarbonylation of the least reactive **7g** as a probe with sodium carboxylates of lower basicities than that of sodium acetate in the expectation that these weak bases might suppress the base-promoted side reactions (*vide supra*). The results are summarized in Table 4. Indeed, with sodium benzoate (run 2), no further palladium black appeared, and the reaction reached completion and provided **8g** in better yield. A similar improvement in the yield and conversion was observed with the use of sodium monochloroacetate as a base (run 3, Table 4), though the reaction became very

(4) Allenyl *endo*-carbamates (e.g., 2,3-butadienyl tosylcarbamate) smoothly undergo palladium(II)-catalyzed aminocarbonylation under the conditions similar to conditions A (in the presence of 3 equiv of sodium monochloroacetate): Kimura, M.; Saeki, N.; Uchida, S.; Harayama, H.; Tanaka, S.; Fugami, K.; Tamaru, Y. *Tetrahedron Lett.* **1993**, *34*, 7611−7614. For the related reaction of 4,5-hexadienylamines, see: Lathbury, D.; Vernon, P.; Gallagher, T. *Tetrahedron Lett.* **1986**, *27*, 6009−6012.

(5) Tamaru, Y.; Tanigawa, H.; Itoh, S.; Kimura, M.; Tanaka, S.; Fugami, K.; Sekiyama, T.; Yoshida, Z. *Tetrahedron Lett.* **1992**, *33*, 631−634. Harayama, H.; Okuno, H.; Takahashi, Y.; Kimura, M.; Fugami, K.; Tanaka, S.; Tamaru, Y. *Tetrahedron Lett.* **1996**, *37*, 7287−7290.

(6) Blackburn, T. F.; Schwaltz, J. *J. Chem. Soc. Chem. Commun.* **1977**, 157−158; Tamaru, Y.; Yamada, Y.; Inoue, K.; Yamamoto, Y.; Yoshida, Z. *J. Org. Chem.* **1983**, *48*, 1286−1292.

**Table 2. Effects of Additives, Bases, and Solvents on Pd(II)-Catalyzed Aminocarbonylation of *endo*-Carbamates 7e[a]**

| run | base (3 mmol) | additive[b] (18 mmol) | solvent | conditions | temp (°C)/ time (h) | conversion (%) | yield (%)[c] **8e** [*trans*:*cis*] |
|---|---|---|---|---|---|---|---|
| 1 | none | none | MeOH | A | 30/74 | 90 | 0 |
| 2 | none | MOA | MeOH | | 30/36 | 100 | 45 [4:1] |
| 3 | AcONa | none | MeOH | | 30/2 | 48[e] | 43 [3:1] |
| 4 | AcONa | AcOH[d] | MeOH[d] | B-1 | 30/72 | 100 | 10 |
| 5 | AcONa | MOA | MeOH | B-2 | 30/8 | 100 | 100 [3:1] |
| 6 | AcONa | MOF | MeOH | | 25/4 | 100 | 94 [3:1] |
| 7 | AcONa | DMP | MeOH | | 25/4 | 100 | 78 [7:1] |
| 8 | none | PO | MeOH | | 25/10 | 100 | 78 [4:1] |
| 9 | none | none | MOA | | 35/3 | 100 | 60 [>20:1] |

[a] Reactions were performed under the following conditions: **7e** (1.0 mmol), $PdCl_2$ (0.25 mmol), and $CuCl_2$ (2.3−3.0 mmol) under CO (1 atm) in MeOH (8 mL) or MOA (5 mL). [b] MOA, trimethyl orthoacetate; MOF, trimethyl orthoformate; DMP, 2,2-dimethoxypropane; PO, propylene oxide. [c] Isolated yield based on conversion. [d] AcOH (5 mL)-MeOH (2 mL). [e] No further reaction owing to precipitation of Pd black.

**Table 3. Pd(II)-Catalyzed Intramolecular Aminocarbonylation of *endo*-Carbamates 7a−h**

| run | **7**: R = | conditions[a] | temp (°C)/ time (h) | conversion (%) | yield of **8** (%)[b] | *trans*:*cis*[c] |
|---|---|---|---|---|---|---|
| 1 | **7a**: H | B-1 | 30/88 | 100 | **8a**: 71 | |
| 2 | | B-2 | 30/2 | 100 | **8a**: 78 | |
| 3 | | B-3′ | 35/20 | 100 | **8a**: 42 | |
| 4 | **7b**: Me | B-1 | 30/87 | 100 | **8b**: 89 | 7:1 |
| 5 | | B-2 | 30/3 | 100 | **8b**: 88 | 2:1 |
| 6 | | B-3′ | 35/18 | 100 | **8b**: 61 | 5:1 |
| 7 | **7c**: Et | B-1 | 30/70 | 100 | **8c**: 80 | 18:1 |
| 8 | | B-2 | 30/5 | 100 | **8c**: 88 | 2:1 |
| 9 | | B-3′ | 35/18 | 100 | **8c**: 46 | 12:1 |
| 10 | **7d**: $CH_2CHMe_2$ | B-1 | 30/93 | 100 | **8d**: 91 | 10:1 |
| 11 | | B-2 | 30/9 | 100 | **8d**: 95 | 2:1 |
| 12 | | B-2′ | 30/23 | 100 | **8d**: 78 | 5:1 |
| 13 | | B-3′ | 35/25 | 100 | **8d**: 70 | >20:1 |
| 14 | **7e**: $CH_2CH_2Ph$ | B-1 | 30/72 | 100 | **8e**: 10 | |
| 15 | | B-2 | 30/8 | 100 | **8e**: 100 | 3:1 |
| 16 | | B-2′ | 35/25 | 100 | **8e**: 90 | 3:1 |
| 17 | | B-3′ | 35/14 | 100 | **8e**: 60 | >20:1 |
| 18 | **7f**: $CHMe_2$ | B-1 | 30/87 | 100 | **8f**: 49 | >20:1 |
| 19 | | B-2 | 30/13 | 87[d] | **8f**: 61 | >20:1 |
| 20 | **7g**: $CMe_3$ | B-1 | 30/91 | 0 | **8g**: 0 | |
| 21 | | B-2 | 30/16 | 50[d] | **8g**: 57 | >20:1 |
| 22 | **7h**: $Me_2$ | B-1 | 30/94 | 100 | **8h**: 14 | |
| 23 | | B-2 | 30/18 | 71[d] | **8h**: 86 | |

[a] See Table 1. [b] Isolated yield based on conversion. [c] Ratio determined by $^1H$ (400 MHz) and/or $^{13}C$ (100 MHz) NMR. [d] No further reaction owing to precipitation of palladium black.

**Table 4. Modification of Reaction Contitions B-2[a] for Unreactive *endo*-Carbamate 7g: Effects of Base and Temperature**

| run | base | p*Ka*[b] | temp (°C)/ time (h) | conversion (%) | yield (%)[c] **8g** [*trans*:*cis*][d] |
|---|---|---|---|---|---|
| 1 | AcONa | 4.75 | 30/16 | 50[e] | 57 [>20:1] |
| 2 | $PhCO_2Na$ | 4.20 | 30/110 | 100 | 77 |
| 3 | $ClCH_2CO_2Na$ | 2.86 | 30/220 | 100 | 77 [>20:1] |
| 4 | $ClCH_2CO_2Na$ | | 65/0.5 | 100 | 65 |
| 5 | $Cl_3CCO_2Na$ | 0.64 | 30/320 | 58 | 58 |

[a] See Table 1. [b] Values of conjugate acid in water. [c] Isolated yield based on conversion. [d] Ratio determined by $^1H$ (400 MHz) and/or $^{13}C$ (100 MHz) NMR. [e] No further reaction owing to precipitation of Pd black.

slow and required an unreasonably prolonged time for completion. The reaction time, however, could be greatly shortened by raising the temperature (run 4, Table 4). A similarly large temperature dependence was observed for the reaction of **7e** using sodium monochloroacetate instead of sodium acetate under conditions B-2, which required 46 h at 30 °C but only 10 min at 65 °C to attain completion (cf. run 15, Table 3). These unusually large increases in rate, ca. 5−6 times by raising the reaction temperature by 10 °C, may most probably be associated with a Pd(0)−$CuCl_2$ redox process, though unfortunately analysis of this process is difficult owing to the heterogeneous nature of the reaction mixture.

The results in Table 4 indicate that the time required for completion of the reaction well corresponds to the base strength: the higher the base strength, and hence the higher the concentration of the conjugate base of **7g**, the shorter the reaction time; the p$K_a$ value of **7g** is ca. 4[7] and is comparable to those of acetic acid and benzoic acid. This suggests that the conjugate base of **7g** is responsible for aminocarbonylation and at the same time this apparently explains why *endo*-carbamates **7** would not undergo aminocarbonylation under conditions A; 2 mol of HCl, generated during the reaction, make the reaction strongly acidic and suppress the dissociation of **7** into its conjugate base.

In order to clarify the mechanistic role of MOA,[8] we examined the reaction of **7e** in the presence of compounds that would undergo C−O bond cleavage upon contact with HCl and would neutralize the HCl evolved during the Wacker-type catalytic cycle (runs 6−9, Table 2). Trimethyl orthoformate (MOF, run 6), 2,2-dimethoxypropane (DMP, run 7), and propylene oxide (PO, run 8),[8] all turned out to work similarly well to improve the yields and conversions.

To our surprise, aminocarbonylation of **7e** smoothly proceeded even in the absence of sodium acetate and methanol; just heating the mixture of **7e** (1 mmol), $PdCl_2$ (0.25 mmol), and $CuCl_2$ (3.0 mmol) in MOA alone at 35 °C for 14 h (run 9, Table 2) was effective. Under these conditions, *trans*-**8e** was produced with remarkably high stereoselectivity (*trans*-**8e**:*cis*-**8e** = >20:1). Interestingly, almost the same results were obtained by using a reduced amount of $PdCl_2$ (0.05 mmol, conditions B-3′, run 17 in Table 3). Conditions B-3′ proved to be successful for the aminocarbonylation of a variety of **7** (runs 3, 6, 9, and 13, Table 3).

These results clearly indicate that MOA works in many ways. MOA promotes the reaction by serving as a base to generate the conjugate base of **7**. At the same time, MOA serves as an efficient scavenger of HCl and keeps the reaction mixture weakly acidic, under which conditions the conjugate base of **7** may be generated in a reasonable concentration and, also, palladium(0) may be oxidized to palladium(II) chloride by copper(II) chloride at a reasonable rate. Furthermore, as a consequence of

(7) Taylor, L. D.; MacDonald, R. J.; Rubin, L. E. *J. Polym. Sci. Part A-1*, **1971**, *9*, 3059−3061.

(8) The use of MOA (and PO) was prompted by our previous experiences; the use of these additives greatly facilitated the Wacker-type dicarbonylation of homoallyl alcohols to provide α-[(methoxycarbonyl)methyl]-γ-butyrolactones: Tamaru, Y.; Hojo, M.; Yoshida, Z. *J. Org. Chem.* **1991**, *56*, 1009−1105.

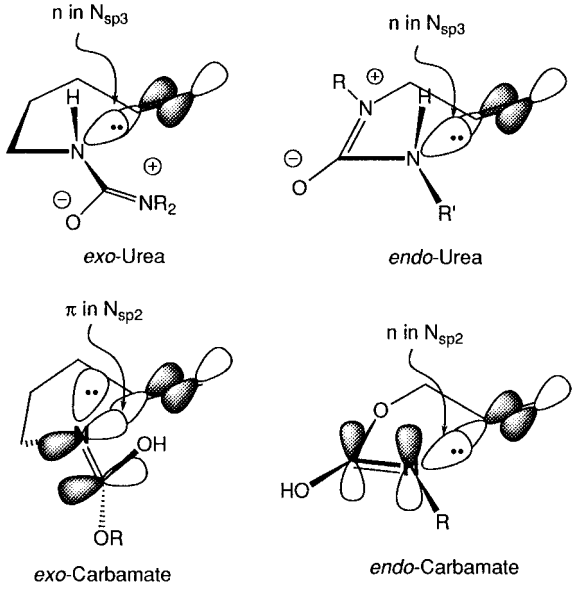



**Figure 1.**

**Table 5. Pd(II)-Catalyzed Aminocarbonylation of 11a−g**[a]

| run | 11 | $R^1$ = | $R^2$ = | conditions[b] | temp (°C)/ time (h) | conversion (%) | yield (%)[c] of **12** | *trans*:*cis*[d] |
|---|---|---|---|---|---|---|---|---|
| 1 | **11a** | H | H | B-1 | 30/89 | 100 | **12a**: 9 | |
| 2 | | | | B-2 | 30/70 | 80[e] | **12a**: 0 | |
| 3 | | | | B-3′ | 65/3 | 100 | **12a**: 12 | |
| 4 | **11b** | Ph | H | B-2[f] | 65/0.5 | 100 | **12b**: 24 | 6:1 |
| 5 | | | | B-3′ | 65/4 | 100 | **12b**: 35 | 2:1 |
| 6 | **11c** | *t*-Bu | H | B-2[f] | 65/0.5 | 100 | **12c**: 53 | 5:1 |
| 7 | | | | B-3′ | 65/2 | 100 | **12c**: 65 | 2:1 |
| 8 | **11d** | $Me_2$ | H | B-2 | 30/15 | 84[e] | **12d**: 37 | |
| 9 | | | | B-2[g] | 65/1 | 100 | **12d**: 70 | |
| 10 | **11e** | $(CH_2)_5$ | H | B-1 | 30/90 | 100 | **12e**: 90 | |
| 11 | **11f**[h] | Ph | Me | B-2[f] | 65/3 | 100 | **12f**: 42[i] | >15:1 |
| 12 | **11g** | $Me_2$ | Me | B-2[f] | 65/2 | 100 | **12g**: 68 | |

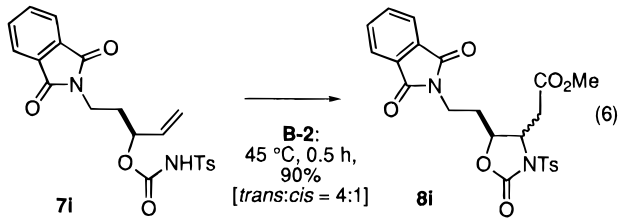
[a] See eqs 8 and 9. [b] See Table 1. [c] Isolated yield based on conversion. [d] Ratio of stereoisomers with respect to $R^1$ and $CH_2CO_2Me$, determined by $^1H$ (400 MHz) and/or $^{13}C$ (100 MHz) NMR. [e] No further reaction owing to precipitation of palladium black. [f] $ClCH_2CO_2Na$ (3 mmol) instead of AcONa. [g] $Cl_3CCO_2Na$ (3 mmol) instead of AcONa. [h] *syn*-**11f**:*anti*-**11f** = 1:1. [i] Isolated yield of **12f** based on *syn*-**11f**.

the reactions with HCl [e.g., $MeC(OMe)_3$ + HCl → $MeCCl(OMe)_2$ + MeOH], MOA supplies the methanol necessary for the methoxycarbonylation of **7**.

The contrasting reactivity of *endo*-carbamates **7** and the other nitrogen nucleophiles **1**, **3**, and **5** may be rationalized as follows (Figure 1). Both *exo*- and *endo*-ureas possess a nonbonding electron pair in an approximately $N_{sp^3}$ orbital that efficiently overlaps with the $\pi^*$ orbital of olefin. An equivalent nucleophilic nitrogen lone pair is not available for both the *endo*- and *exo*-carbamates owing to their approximate $N_{sp^2}$ hybridization. Nevertheless, *exo*-carbamates may still be reactive owing to an efficient overlap between the $\pi^*$ orbital of olefin and the nucleophilic enol-like C=N $\pi$ orbital. In the case of *endo*-carbamates, however, the nitrogen lone pair in the $N_{sp^2}$ orbital that efficiently overlaps with the $\pi^*$ orbital of olefin may not be sufficiently nucleophilic and may become suitably reactive only when its nucleophilicity is enhanced by dissociation into the conjugate base.[9]

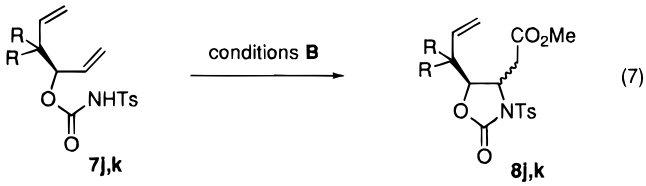
(9) For a similar stereoelectronic effect on cyclization reactions, see: McCombie, S. M.; Shankar, B. B.; Ganguly, A. K. *Tetrahedron Lett.* **1985**, *26*, 6301−6304.

The synthetic utility of the present reaction may be demonstrated by the transformation of **7i** into **8i** (eq 6).



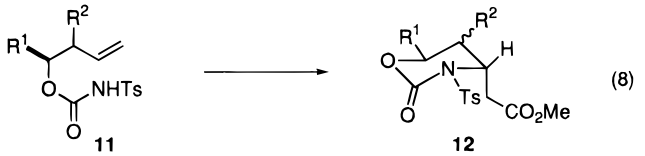

The product **8i** is a protected form of $\gamma$-hydroxy-$\beta$-lysine, an unusual amino acid isolated from tuberactinomycin A and N.[10]

**Aminocarbonylation of 3-Butenyl Carbamates 11.** The selective transformation of **7j** and **7k** into **8j** and **8k** (eq 7), respectively, clearly indicates that the aminocarbonylation forming five-membered cyclic carbamates




**7j** (R = H) B-2: 30 °C, 6 h **8j** (R = H): 64% [*trans*:*cis* = 5:1]
B-3: 35 °C, 20 h **8j** (R = H): 66% [*trans*:*cis* = 15:1]

**7k** (R = Me) B-2: 35 °C, 6 h **8k** (R = Me): 70% [*trans*:*cis* = >20:1]




proceeds much faster than the alternative reaction forming six-membered cyclic carbamates. Indeed, the reaction forming six-membered cyclic carbamates (eq 8) was generally rather slow. Results obtained for the aminocarbonylation of 3-butenyl carbamates **11a**−**g** are summarized in Table 5.

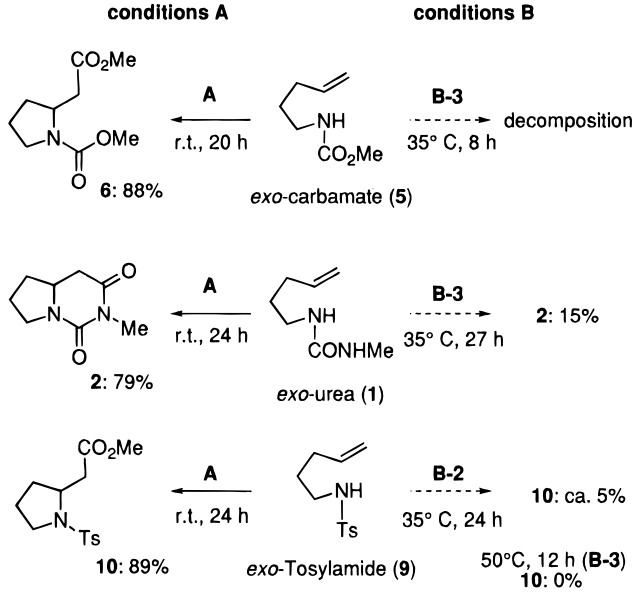
Among **11**, the parent **11a** was exceedingly unreactive and the expected product **12a** was obtained in very poor yields, if at all (runs 1−3, Table 5). The C-1 monosubstituted derivatives, **12b**,**c**,**f**, were slightly more reactive and provided the expected products in moderate yields under the modified conditions B-2 (sodium monochloroacetate in place of sodium acetate), the conditions being successful for the unreactive **7g** (runs 3 and 4, Table 4). Under the usual conditions B-2, utilizing sodium acetate as a base, these reactions hardly reached completion owing to precipitation of palladium black. Slightly better yields resulted under conditions B-3′.

In these reactions, *trans*-isomers, being *trans* with respect to $R^1$ and (methoxycarbonyl)methyl groups, were obtained as the major isomers. This is probably because *cis*-**12** is thermodynamically less stable owing to an $A^{1,2}$-strain between the tosyl and the *pseudo-equatorial* methoxycarbonyl groups.[11]

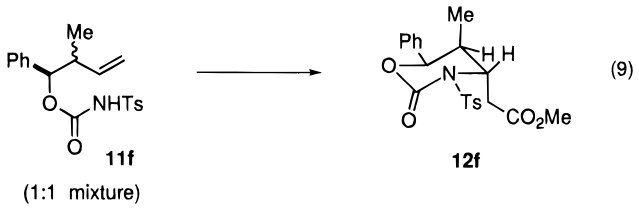
(10) Wakamiya, T.; Shiba, T.; Kaneko, T. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 3668−3672.

(11) (a) Hoffmann, R. W. *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1124−1134. (b) Bando, T.; Harayama, H.; Fukazawa, Y.; Shiro, M.; Fugami, K.; Tanaka, S.; Tamaru, Y. *J. Org. Chem.* **1994**, *59*, 1465−1474.

**Scheme 1**




Only the *syn* isomer of the mixture of *syn*- and *anti*-**11f** (1:1) underwent aminocarbonylation to selectively furnish *trans*,*cis*-4-[(methoxycarbonyl)methyl]-5-methyl-6-phenyl-*N*-tosyltetrahydro-2-oxazinone (**12f**) in 42% yield (based on *syn*-**11f**, eq 9). The *anti*-isomer of **11f** decomposed completely during the reaction.




The C-1 disubstituted derivatives, **11d**,**e**,**g**, were much more reactive and provided the expected products in moderate to good yields (runs 8−10 and 12, Table 5). These C-1 substituents of **11** may accelerate the reaction by buttressing both reaction sites (carbamate nitrogen and C-3) to bring them into closer proximity.[12]

The aminocarbonylation of **11** seems to be useful for the synthesis of naturally occurring $\beta$-amino-$\delta$-hydroxy acids, e.g., negamycin.[13]

**Chemoselective Aminocarbonylation of *endo*-Carbamates and the Other Nitrogen Nucleophiles.** As summarized in Scheme 1, under conditions B established for the aminocarbonylation of *endo*-carbamates, the other nitrogen nucleophiles reacted very sluggishly, either providing the expected products in poor yields after prolonged reaction times or only giving rise to decomposition products. For example, *exo*-carbamate **5** completely decomposed under conditions B-3. Under conditions B-2, *exo*-tosylamide **9** provided the aminocarbonylation product **10** in 5% isolated yield after heating at 30 °C for 1 day with recovery of **9** in 65% yield, these results being in sharp contrast to the complete conversion of *endo*-carbamate **7a** into **8a** (78% yield, run 2 in Table 3) under the same conditions within 2 h.

(12) Kimura, M.; Tanaka, S.; Tamaru, Y. *J. Org. Chem.* **1995**, *60*, 3764−3772.

(13) Wang, Y.-F.; Izawa, T.; Kobayashi, S.; Ohno, M. *J. Am. Chem. Soc.* **1982**, *104*, 6465−6466; Masters, J. J.; Hegedus, L. S. *J. Org. Chem.* **1993**, *58*, 4547−4554.

**Scheme 2. Chemoselective Aminocarbonylation of 7n−q**

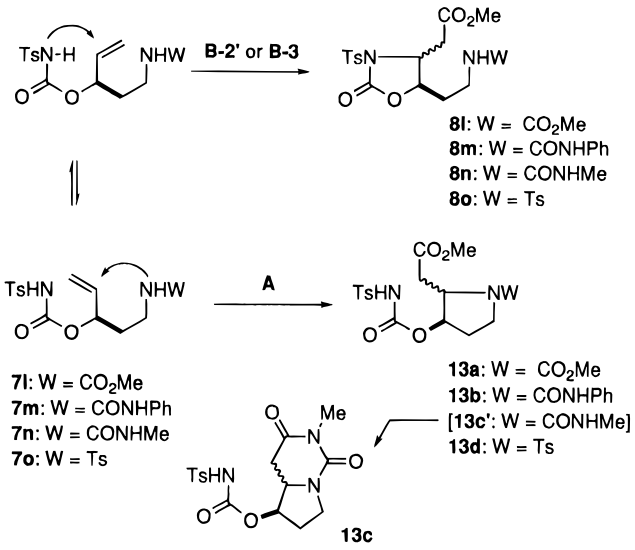



**Table 6. Chemoselective Aminocarbonylation of 7n−q[a]**

| run | 7: W = | conditions[b] | temp (°C)/ time (h) | % isolated yield[c] 8 [*trans*:*cis*][d] | % isolated yield[c] 13 [*trans*:*cis*][d] |
|---|---|---|---|---|---|
| 1 | **7l**: $CO_2Me$ | B-2′ | 25/35 | **8l**: 74 [3:1] | |
| 2 | | B-3 | 35/7 | **8l**: 68 [11:1] | |
| 3 | | A | 25/120 | | **13a**: 58 [1:3] |
| 4 | **7m**: CONHPh | B-2′ | 25/20 | **8m**: 85 [11:1] | |
| 5 | | B-3 | 35/6 | **8m**: 45 [>20:1] | |
| 6 | | A | 25/120 | | **13b**: 36 [1:4] |
| 7 | **7n**: CONHMe | B-2′ | 25/48 | **8n**: 85 [5:1] | |
| 8 | | A | 25/22 | | **13c**: 59 [1:1] |
| 9 | **7o**: Ts | B-2′ | 25/17 | **8o**: 78 [3:1] | |
| 10 | | B-3 | 25/17 | **8o**: 60 [20:1] | |
| 11 | | A | 25/72 | | **13d**: 79 [1:3] |

[a] For the structure of **7n−q**, **8n−q**, and **13a−d**, see Scheme 2. [b] See Table 1. [c] 100% conversion for all cases. [d] Ratio determined by $^1$H (400 MHz) and/or $^{13}$C (100 MHz) NMR.

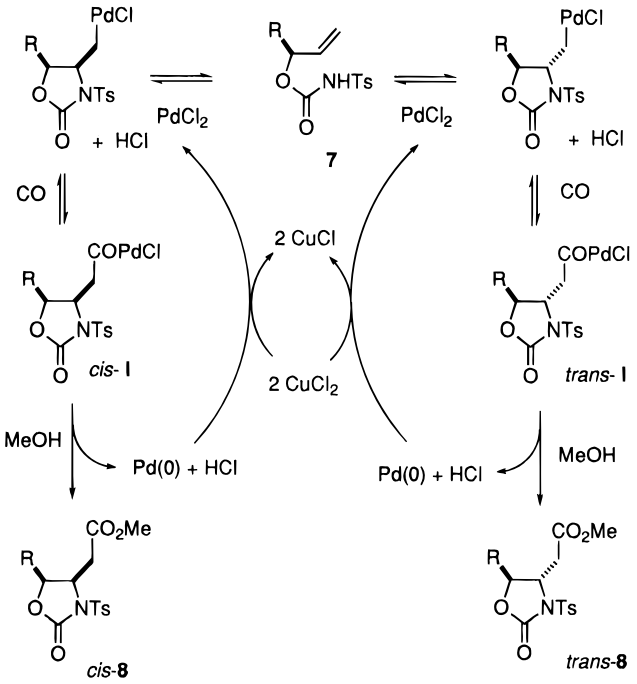
This clear-cut congeniality between the structure type of nitrogen nucleophiles and reaction conditions suggests that **7l** assembled with two types of nitrogen nucleophiles (*endo*- and *exo*-carbamate) would undergo aminocarbonylation chemoselectively just by changing the reaction conditions (Scheme 2). Indeed, the *endo*-carbamate moiety of **7l** selectively underwent aminocarbonylation under buffered conditions B-2′ and B-3 to provide **8l** in good yields (runs 1,2, Table 6). On the other hand, the *exo*-carbamate moiety of **7l** reacted selectively under acidic conditions A to give rise to **13a** in reasonable yield (run 3, Table 6).

A similarly distinctive chemoselective cyclization was observed for substrates possessing *endo*-carbamate and *exo*-urea (**7m**,**n**, runs 4−8, Table 6) and *endo*-carbamate and *exo*-tosylamide moieties (**7o**, runs 9−11, Table 6). In these experiments, the chemoselectivities were complete, and **8l−o** and **13a−d** were obtained exclusively.

The reaction of **7n** under conditions A (run 8) furnished the bicyclic product **13c**, which presumably was formed via further imidation of the primary product **13c′**.

*trans*-Selective formation of **8l−o** is usual. *cis*-Selective formation of **13a−d** seems to be unusual on steric grounds; however, this is in good accord with our previous observation that palladium(II)-catalyzed aminocarbonylation of 3-hydroxy-4-pentenyl carbamates[3] and 3-hydroxy-4-pentenols[14] provides *cis*-3-hydroxypyrrolidine 2-acetic acid lactones and *cis*-3-hydroxytetrahydrofuran

**Scheme 3**




2-acetic acid lactones, respectively, in good yields with excellent stereoselectivities. Judging from these two and many other related examples,[15] the allylic oxygen atom of **7o**−**l** seems to be responsible for the *cis*-selective formation of **13a**−**d**.

Finally, it should be emphasized that the chemoselective aminocarbonylation of *endo*-carbamates and the other nitrogen nucleophiles of **7l**−**o** could be achieved just by changing the reaction medium: at the *endo*-carbamate moiety in MOA alone (conditions B-3) and at the other nitrogen nucleophiles in methanol alone (conditions A).

**Dependence of Stereoselectivity on Reaction Conditions.** The aminocarbonylation of **7** shows an interesting correlation between the stereoselectivity of *cis*- and *trans*-**8** and reaction conditions (Tables 3 and 6 and eq 7): in general, *trans*-**8's** are produced in the highest proportions under conditions B-1, in nearly equal or slightly lower proportions under conditions B-3 (and B-3′) and in the lowest proportions under conditions B-2 (and B-2′). The dependence of stereoselectivity on the reaction conditions may be rationalized according to a plausible catalytic cycle shown in Scheme 3, which involves an equilibrium between acylpalladium intermediates *cis*- and *trans*-**I** and an irreversible transformation of these complexes into the final products *cis*- and *trans*-**8**.[16] Through this equilibrium, *trans*-**I** may accumulate at the expense of *cis*-**I**, owing to the higher thermodynamic stability of the former than the latter.

Under conditions B-1, methanol is poorly nucleophilic, being present as MeOH (2 mL) diluted with AcOH (8 mL), and *cis*-**I** and *trans*-**I** are allowed to equilibrate, leading to thermodynamic control, and hence high *trans*-selectivities. Similarly high *trans*-selectivities under conditions B-3 (and B-3′) seem to be a natural consequence of the presence of methanol in a limited amount. Theoretically, 2 equiv at most of methanol should be present, which corresponds to the amount of HCl evolved. Practically, however, slightly more methanol may be present, since water, contained in inorganic reagents, may produce methanol by hydrolysis of MOA.

Under conditions B-2, on the other hand, methanol is more nucleophilic, being present as a neat solvent, and hinders the equilibrium. Accordingly, the reaction becomes more kinetically controlled, resulting in the lower *trans*-selectivities.

The structure of *cis*- and *trans*-**8** was elucidated by $^{13}C$ NMR, where the α-carbons of substituents attached to C-4 and C-5 of *cis*-**8** showed higher field resonances by ca. 5 ppm as compared with those of *trans*-**8**, and/or by $^{1}H$ NMR, where *cis*-**8** showed $^{3}J_{H4-H5}$ = ca. 7 Hz, while *trans*-**8** $^{3}J_{H4-H5}$ = ca. 3 Hz.[17] The structure of **12** was determined by comparison of the coupling patterns of tetrahydro-2-oxazolidinone ring protons with those of the structurally related compounds[11b] as well as by NOE experiments (see Experimental Section).

## Conclusion

Among nitrogen nucleophiles, *endo*-carbamates display distinctive reactivity for the Wacker-type aminocarbonylation. Many nitrogen nucleophiles (*exo*-carbamates, *endo*-ureas, *exo*-ureas, and *exo*-tosylamides) smoothly undergo aminocarbonylation under conditions A, but not under conditions B. *endo*-Carbamates, on the other hand, react under conditions B and not under conditions A. Conditions A are strongly acidic, since 2 mol of HCl evolve during the catalytic cycle, while conditions B are buffered, since the HCl evolved is neutralized either by a base (NaOAc, etc.) or by MOA. Conditions B are sufficiently basic to generate the conjugate base of *endo*-carbamates, a reactive species for aminocarbonylation, but not so basic as to cause undesirable $PdCl_2$-mediated side reactions. Conditions B-3 (and B-3′) that can be successfully applied to a wide variety of *endo*-carbamates **7** and **11** are only different from conditions A in the solvent utilized, MOA for the former and MeOH for the latter. By applying these conditions A and B, completely chemoselective aminocarbonylation of **7l**−**o**, at the *endo*-carbamate moieties under conditions B and at the other nitrogen nucleophiles under conditions A, can be achieved.

The aminocarbonylation reported here may find wide application in the synthesis of γ- and δ-hydroxy-β-amino acids and their derivatives of structural complexity.[10,13]

## Experimental Section

Melting points are not corrected. Unless otherwise specified, short-path (bulb-to-bulb) distillations were carried out in a Kugelrohr apparatus. In these cases, boiling points refer to the oven temperature. Microanalyses were performed by the Microanalysis Center of Nagasaki University. Analyses agreed with the calculated values within ±0.3%. Proton magnetic resonance spectra were determined either at 60, 90, or 400 MHz with TMS as an internal standard. Carbon magnetic resonance spectra were recorded at 22.5, 75, or 100 MHz. Chemical shift values were given in ppm downfield from TMS. $R_f$ values were measured with Merck Kieselgel $60F_{254}$.

(14) Tamaru, Y.; Kobayashi, T.; Kawamura, S.; Ochiai, H.; Hojo, M.; Yoshida, Z. *Tetrahedron Lett.* **1985**, *26*, 3207−3210.

(15) (a) Tamaru, Y.; Higashimura, H.; Naka, K.; Hojo, M.; Yoshida, Z. *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 1045−1046. (b) Tamaru, Y.; Hojo, M.; Kawamura, S.; Sawada, S.; Yoshida, Z. *J. Org. Chem.* **1987**, *52*, 4062−4072. (c) Tamaru, Y.; Kawamura, S.; Bando, T.; Tanaka, K.; Hojo, M.; Yoshida, Z. *J. Org. Chem.* **1988**, *53*, 5491−5501. (d) Tamaru, Y.; Harayama, H.; Bando, T.; Nagaoka, H.; Yoshida, Z. *Liebigs Ann.* **1996**, 223−234.

(16) For the related discussion, see: Nilsson, Y. I. M.; Aranyos, A.; Andersson, P. G.; Bäckvall, J.-E.; Parrain, J.-L.; Plateau, C.; Quintard, J.-P. *J. Org. Chem.* **1996**, *61*, 1825−1829.

(17) Breitmaier, E. *Structure Elucidation by NMR in Organic Chemistry*; Wiley: New York, 1993.

**Solvents and Reagents.** THF and ether were dried and distilled from benzophenone sodium ketyl immediately before use under nitrogen. Triethylamine was distilled over $CaH_2$. Methanol was dried and distilled from Mg and $I_2$ under nitrogen. Acetic acid was distilled from $P_2O_5$. MOA, MOF, and DMP were distilled from Na under $N_2$ under atmospheric pressure. Methyl isocyanate, phenyl isocyanate, and methyl chlorocarbonate were used without purification. Tosyl isocyanate was distilled prior to use (120 °C/0.5 Torr). Acrolein was distilled from $CaSO_4$ in the presence of a small amount of *p*-methoxyphenol under $N_2$. $PdCl_2$, $CuCl_2$, AcONa, $PhCO_2Na$, $ClCH_2CO_2Na$, $Cl_3CCO_2Na$, boron trifluoride etherate, and allylmagnesium chloride (2.0 M in THF) were purchased and used without purification. *Caution! Benzene is highly toxic. All operations (TLC monitoring and recrystallization) with this solvent should be carried out in a well-ventilated hood. In most cases, benzene may be substituted with other solvents (e.g., toluene).*

**2-Propenyl Tosylcarbamates 7a−k.** Carbamates **7a−k** were prepared by the reaction of tosyl isocyanate and the corresponding 2-propen-1-ols according to the procedure reported from our laboratories.[18] 2-Propen-1-ol, 1-methyl-2-propen-1-ol, 1,1-dimethyl-2-propen-1-ol were purchased and used without purification. 1-Penten-3-ol, 4-methyl-1-penten-3-ol, 4,4-dimethyl-1-penten-3-ol, and 1,5-hexadien-3-ol were prepared by the reaction of acrolein with the appropriate Grignard reagents (ether, 0 °C). 4,4-Dimethyl-1,5-hexadien-3-ol was prepared as follows: A solution of 3,3-dimethyl-2-propenyl bromide (50 mmol) in THF (80 mL) was added dropwise over 3 h into well-stirred suspension of Zn−Cu couple (55 mmol) over THF (20 mL) at −20 °C under $N_2$. The mixture was stirred for an additional 1 h at −20 °C. Into this mixture was added acrolein (75 mmol) dissolved in ether (70 mL) at −20 °C over 2 h. After stirring for an additional 2 h at room temperature, the mixture was poured into ether (100 mL) and the mixture was washed with 2 M HCl (40 mL), brine (20 mL), and then with saturated $NaHCO_3$. The organic layer was dried ($MgSO_4$), filtered, and concentrated to give an oil, which was distilled under reduced pressure (55 °C/10 Torr, 70% yield).

**2-Propenyl Tosylcarbamates 7l−o.** Into a stirred solution of methyl 3-hydroxy-4-pentenylcarbamate (10 mmol)[15c] in THF (20 mL) kept at 0 °C was added dropwise boron trifluoride etherate (10 mmol) and then tosyl isocyanate (10 mmol) via syringes. After stirring for 1 h at 0 °C, the temperature was allowed to rise to room temperature and the mixture was stirred for an additional 1 h. The mixture was diluted with ethyl acetate (100 mL) and washed with saturated $NaHCO_3$. The organic phase was dried ($MgSO_4$), filtered, and concentrated. The residue was chromatographed over silica gel (toluene−ethyl acetate gradient) to give **7l** in 60% yield; $R_f$ = 0.55 (benzene−ethyl acetate = 1/1, v/v). According to the similar procedure, **7m** [56% after purification by column chromatography over silica gel, ethyl acetate−acetone gradient; $R_f$ = 0.6 (acetone−ethyl acetate = 2/1, v/v)], **7n** [49% after purification by column chromatography over silica gel, ethyl acetate−acetone gradient; $R_f$ = 0.45 (acetone−ethyl acetate = 2/1, v/v)], and **7o** [100% after purification by column chromatography over silica gel, toluene−ethyl acetate gradient; $R_f$ = 0.5 (benzene−ethyl acetate = 2/1, v/v)] were prepared from *N*-phenyl-*N*′-(3-hydroxy-4-pentenyl)urea,[15c] *N*-methyl-*N*′-(3-hydroxy-4-pentenyl)urea,[15c] and *N*-tosyl-3-hydroxy-4-pentenylamine,[15c] respectively.

**3-Butenyl Tosylcarbamates 11a−g.** Carbamates **11a−g** were prepared by the reaction of tosyl carbamate and the corresponding 3-buten-1-ols according to the procedure reported from our laboratories.[18] 3-Buten-1-ol was purchased and the other 3-buten-1-ols were prepared as follows: 1-Phenyl-3-buten-1-ol (benzaldehyde and allylmagnesium chloride), 1-*tert*-butyl-3-buten-1-ol (trimethylacetaldehyde and allylmagnesium chloride), 1,1-dimethyl-3-buten-1-ol (acetone and allylmagnesium chloride), 1-allylcyclohexan-1-ol (cyclohexanone and allylmagnesium chloride), 2-methyl-1-phenyl-3-penten-1-ol (benzaldehyde and 2-butenylmagnesium chloride), and 1,1,2-trimethyl-3-buten-1-ol (acetone and 2-butenylmagnesium chloride).

**Aminocarbonylation of 7 and 11.** The aminocarbonylation of **7** and **11** under conditions A and B was performed essentially in the same way as typified by the following reactions of **7l**.

**Aminocarbonylation of 7l under Conditions B-3 (run 2, Table 6).** Into a flask containing $PdCl_2$ (0.1 mmol) and $CuCl_2$ (2.3 mmol), purged with carbon monoxide (a balloon), was added **7l** (1 mmol) dissolved in trimethyl orthoacetate (5 mL) via a syringe. The mixture was stirred at 35 °C for 7 h, during which time the reaction was monitored by TLC ($R_{f7l}$ = 0.55, $R_{f8l}$ = 0.65, benzene−ethyl acetate = 1/1, v/v). The mixture was diluted with ethyl acetate (50 mL) and washed with 5% $NH_4Cl$−5% $NH_3$ (2 × 15 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The residue was chromatographed over silica gel (hexane−ethyl acetate gradient) to give a mixture of *trans*- and *cis*-**8l** (11:1) in 68% yield. Pure *trans*-**8l** was obtained by recrystallization from dichloromethane−hexane.

**Aminocarbonylation of 7l under Conditions A (run 3, Table 6).** Into a flask containing $PdCl_2$ (0.1 mmol) and $CuCl_2$ (3.0 mmol), purged with carbon monoxide (a balloon), was added **7l** (1 mmol) dissolved in methanol (5 mL) via a syringe. The mixture was stirred at 25 °C for 120 h, during which time the reaction was monitored by TLC ($R_{f7l}$ = 0.55, $R_{f13a}$ = 0.50, benzene−ethyl acetate = 1/1, v/v). After evaporation of the solvent, the residue was diluted with ethyl acetate and filtered through a Celite pad on a funnel. The filtrate was concentrated and the residue was chromatographed over silica gel (toluene−ethyl acetate gradient) to provide a mixture of *trans*- and *cis*-**13a** (1:3) in 58% yield. Pure *cis*-**13a** was obtained by recrystallization from dichloromethane−hexane.

**1-Benzyl-4-[(methoxycarbonyl)methyl]-3-propyl-2-imidazolidinone (4)**: oil; IR (neat film) 1780 (s), 1690 (s) $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 0.91 (t, $J$ = 7.4 Hz, 3 H), 1.48−1.58 (m, 2 H), 2.39 (dd, $J$ = 9.1, 16.0 Hz, 1 H), 2.74 (dd, $J$ = 4.1, 16.0 Hz, 1 H), 2.87−2.98 (m, 2 H), 3.38−3.45 (m, 2 H), 3.66 (s, 3 H), 3.93 (m, 1 H), 4.32 (d, $J$ = 15.0 Hz, 1 H), 4.40 (d, $J$ = 15.0 Hz, 1 H), 7.23−7.35 (m, 5 H); HRMS calcd for $C_{16}H_{22}N_2O_3$ 290.1630, found *m*/*z* (relative intensity) 290.1625 ($M^+$, 76.4), 262.1 (17.5), 261.1 (100.0), 218.1 (8.7), 217.1 (68.1), 199.1 (7.8).

**1-(Methoxycarbonyl)-2-[(methoxycarbonyl)methyl]pyrrolidine (6)**: oil; IR (neat film) 1740 (m), 1700 (s) $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO-$d_6$, 100 °C) $\delta$ 1.68 (m, 1 H), 1.73−1.89 (m, 2 H), 2.01 (m, 1 H), 2.37 (dd, $J$ = 8.8, 15.0 Hz, 1 H), 2.69 (dd, $J$ = 4.0, 15.0 Hz, 1 H), 3.24−3.36 (m, 2 H), 3.58 (s, 3 H), 3.60 (s, 3 H), 4.04 (tt, $J$ = 4.0, 8.8 Hz, 1 H); HRMS calcd for $C_9H_{15}NO_4$ 201.1001, found *m*/*z* (relative intensity) 201.1001 ($M^+$, 24.8), 170.1 (10.9), 142.1 (47.3), 128.1 (100.0), 110.1 (5.0), 82.1 (5.1).

**4-[(Methoxycarbonyl)methyl]-3-tosyl-2-oxazolidinone (8a)**: mp 120.5−121.1 °C (benzene−hexane); IR (KBr disk) 1770 (s), 1730 (s), 1725 (s) $cm^{-1}$; $^1H$ NMR (90 MHz, $CDCl_3$) $\delta$ 2.45 (s, 3 H), 2.77 (dd, $J$ = 9.3, 16.9 Hz, 1 H), 3.31 (dd, $J$ = 3.4, 16.9 Hz, 1 H), 3.70 (s, 3 H), 4.13 (dd, $J$ = 4.0, 8.7 Hz, 1 H), 4.41−4.88 (m, 2 H), 7.35 (d, $J$ = 8.5 Hz, 2 H), 7.94 (d, $J$ = 8.5 Hz, 2 H); $^{13}C$ NMR (22.5 MHz, $CDCl_3$) $\delta$ 21.3, 38.1 ($CH_2CO_2$-Me), 51.7 ($CO_2CH_3$), 53.2 ($C_4$), 67.8 ($C_5$), 128.2, 129.6, 134.7, 145.5, 151.7 ($C_2$), 169.6 ($CO_2$Me). Anal. Calcd for $C_{13}H_{15}NO_6S$: C, 49.83; H, 4.83; N, 4.47; S, 10.23. Found: C, 49.76; H, 4.81; N, 4.45; S, 10.20.

***trans*-4-[(Methoxycarbonyl)methyl]-5-methyl-3-tosyl-2-oxazolidinone (8b)**: mp 83.0−84.5 °C (benzene−hexane); IR (KBr disk) 1780 (s), 1720 (s) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.35 (d, $J$ = 6.2 Hz, 3 H), 2.46 (s, 3 H), 2.77 (dd, $J$ = 9.9, 17.2 Hz, 1 H), 3.19 (dd, $J$ = 2.9, 17.2 Hz, 1 H), 3.71 (s, 3 H), 4.29 (dt, $J$ = 9.9, 2.9 Hz, 1 H), 4.41 (dq, $J$ = 2.9, 6.2 Hz, 1 H), 7.37 (d, $J$ = 8.4 Hz, 2 H), 7.94 (d, $J$ = 8.4 Hz, 2 H); $^{13}C$ NMR (22.5 MHz, $CDCl_3$) $\delta$ 20.3 ($CHCH_3$), 21.3, 38.0 ($CH_2CO_2$-Me), 51.7 ($CO_2CH_3$), 59.5 ($C_4$), 76.6 ($C_5$), 128.0, 129.6, 134.8, 145.5, 150.1 ($C_2$), 169.6 ($CO_2$Me). [*cis*-**8b**: $^1H$ NMR (400 MHz,

(18) Tamaru, Y.; Kimura, M.; Tanaka, S.; Kure, S.; Yoshida, Z. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 2838−2849.

$CDCl_3$) $\delta$ 1.32 (d, $J$ = 6.2 Hz, 3 H), 2.45 (s, 3 H), 2.84 (dd, $J$ = 9.5, 17.2 Hz, 1 H), 3.10 (dd, $J$ = 2.9, 17.2 Hz, 1 H), 3.70 (s, 3 H), 4.75−4.85 (m, 2 H), 7.32 (d, $J$ = 8.4 Hz, 2 H), 7.82 (d, $J$ = 8.4 Hz, 2 H); $^{13}$C NMR (22.5 MHz, $CDCl_3$) $\delta$ 14.1 (CH*C*H$_3$), 21.3, 33.7 (*C*H$_2$CO$_2$Me), 51.7 (CO$_2$*C*H$_3$), 56.8 (C$_4$), 74.5 (C$_5$), 128.0, 129.6, 134.8, 145.5, 150.1 (C$_2$), 169.6 (*C*O$_2$Me).] Anal. Calcd for $C_{14}H_{17}NO_6S$: C, 51.37; H, 5.23; N, 4.28; S, 9.79. Found: C, 51.38; H, 5.36; N, 4.30; S, 9.91.

***trans*-5-Ethyl-4-[(methoxycarbonyl)methyl]-3-tosyl-2-oxazolidinone (8c)**: mp 77.7−78.0 °C (benzene−hexane); IR (KBr disk) 1780 (s), 1740 (s) cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 0.91 (t, $J$ = 7.3 Hz, 3 H), 1.54−1.76 (m, 2 H), 2.46 (s, 3 H), 2.80 (dd, $J$ = 9.5, 16.9 Hz, 1 H), 3.17 (dd, $J$ = 3.3, 16.9 Hz, 1 H), 3.70 (s, 3 H), 4.23 (ddd, $J$ = 3.3, 4.7, 7.3 Hz, 1 H), 4.36 (dt, $J$ = 9.5, 3.3 Hz, 1 H), 7.36 (d, $J$ = 8.4 Hz, 2 H), 7.94 (d, $J$ = 8.4 Hz, 2 H); NOEs for H$_5$ (0.0%) and one of methylene protons of ethyl group (3.3%) by irradiation of the signal of H$_4$; $^{13}$C NMR (22.5 MHz, $CDCl_3$) $\delta$ 7.9 (CH$_2$*C*H$_3$), 21.3, 27.4 (*C*H$_2$CH$_3$), 38.2 (*C*H$_2$CO$_2$Me), 51.6 (CO$_2$*C*H$_3$), 57.5 (C$_4$), 80.9 (C$_5$), 128.0, 129.5, 134.8, 145.4, 151.0 (C$_2$), 169.5 (*C*O$_2$Me). [*cis*-**8c**: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.02 (t, $J$ = 7.3 Hz, 3 H), 1.54−1.76 (m, 2 H), 2.42 (s, 3 H), 2.85 (dd, $J$ = 9.7, 17.2 Hz, 1 H), 3.02 (dd, $J$ = 3.3, 17.2 Hz, 1 H), 3.68 (s, 3 H), 4.50 (ddd, $J$ = 3.3, 7.3, 9.7 Hz, 1 H), 4.83 (ddd, $J$ = 3.3, 7.3, 10.6 Hz, 1 H), 7.35 (d, $J$ = 8.4 Hz, 2 H), 7.95 (d, $J$ = 8.4 Hz, 2 H).] Anal. Calcd for $C_{15}H_{19}NO_6S$: C, 52.78; H, 5.61; N, 4.10; S, 9.39. Found: C, 52.87; H, 5.58; N, 4.14; S, 9.57.

***trans*-5-Isobutyl-4-[(methoxycarbonyl)methyl]-3-tosyl-2-oxazolidinone (8d)**: oil; IR (neat film) 1785 (s), 1735 (s) cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 0.89 (d, $J$ = 6.6 Hz, 6 H), 1.41 (ddd, $J$ = 4.8, 8.4, 14.3 Hz, 1 H), 1.47 (ddd, $J$ = 5.5, 9.2, 14.3 Hz, 1 H), 1.76 (m, 1 H), 2.46 (s, 3 H), 2.78 (dd, $J$ = 9.2, 17.2 Hz, 1 H), 3.15 (dd, $J$ = 3.3, 17.2 Hz, 1 H), 3.70 (s, 3 H), 4.29 (dt, $J$ = 9.2, 3.3 Hz, 1 H), 4.34 (ddd, $J$ = 3.3, 4.8, 9.2 Hz, 1 H), 7.37 (d, $J$ = 8.4 Hz, 2 H), 7.93 (d, $J$ = 8.4 Hz, 2 H); $^{13}$C NMR (22.5 MHz, $CDCl_3$) $\delta$ 21.4, 21.6, 22.7, 23.9, 38.2 (*C*H$_2$-CO$_2$Me), 43.6 (*C*H$_2$-*i*-Bu), 51.7 (CO$_2$*C*H$_3$), 58.6 (C$_4$), 78.8 (C$_5$), 128.2, 129.6, 135.0, 145.5, 151.0 (C$_2$), 169.6 (*C*O$_2$Me). [*cis*-**8d**: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 0.88 (d, $J$ = 6.6 Hz, 6 H), 1.37−1.50 (m, 2 H), 1.76 (m, 1 H), 2.45 (s, 3 H), 2.77 (dd, $J$ = 9.2, 17.2 Hz, 1 H), 2.99 (dd, $J$ = 3.3, 17.2 Hz, 1 H), 3.68 (s, 3 H), 4.67 (ddd, $J$ = 3.3, 7.3, 11.0 Hz, 1 H), 4.82 (ddd, $J$ = 3.3, 7.3, 9.2 Hz, 1 H), 7.33 (d, $J$ = 8.4 Hz, 2 H), 7.92 (d, $J$ = 8.4 Hz, 2 H).] HRMS calcd for $C_{17}H_{23}NO_6S - CH_3$ 354.1012, found *m*/*z* (relative intensity), 354.1018 ($M^+ - CH_3$, 1.0), 338.0 (1.0), 232.0 (6.0), 214.0 (12.0), 155.0 (21.0), 108.0 (100.0).

***trans*-4-[(Methoxycarbonyl)methyl]-5-(2-phenylethyl)-3-tosyl-2-oxazolidinone (8e)**: mp 125.0−126.0 °C (benzene−hexane); IR (KBr disk) 1790 (s), 1730 (s) cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.82 (dddd, $J$ = 4.0, 5.1, 9.2, 14.3 Hz, 1 H), 1.97 (ddt, $J$ = 9.9, 14.3, 7.0 Hz, 1 H), 2.43 (s, 3 H), 2.60 (ddd, $J$ = 7.0, 9.2, 13.9 Hz, 1 H), 2.68 (ddd, $J$ = 5.1, 9.9, 13.9 Hz, 1 H), 2.75 (dd, $J$ = 9.9, 16.9 Hz, 1 H), 3.16 (dd, $J$ = 3.3, 16.9 Hz, 1 H), 3.65 (s, 3 H), 4.25 (ddd, $J$ = 3.3, 4.0, 7.0 Hz, 1 H), 4.35 (dt, $J$ = 9.9, 3.0 Hz, 1 H), 7.10 (d, $J$ = 7.3 Hz, 2 H), 7.19 (t, $J$ = 7.3 Hz, 1 H), 7.27 (t, $J$ = 7.3 Hz, 2 H), 7.35 (d, $J$ = 8.1 Hz, 2 H), 7.93 (d, $J$ = 8.1 Hz, 2 H). Anal. Calcd for $C_{21}H_{23}NO_6S$: C, 60.42; H, 5.55; N,3.36; S, 7.68. Found: C, 60.70; H, 5.53; N, 3.38; S, 7.53.

***trans*-5-Isopropyl-4-[(methoxycarbonyl)methyl]-3-tosyl-2-oxazolidinone (8f)**: mp 96.4−96.6 °C (benzene−hexane); IR (KBr disk) 1770 (s), 1745 (s) cm$^{-1}$; $^1$H NMR (90 MHz, $CDCl_3$) $\delta$ 0.82 (d, $J$ = 6.8 Hz, 3 H), 0.92 (d, $J$ = 6.8 Hz, 3 H), 1.86 (m, 1 H), 2.45 (s, 3 H), 2.80 (dd, $J$ = 8.5, 16.6 Hz, 1 H), 3.11 (dd, $J$ = 3.7, 16.6 Hz, 1 H), 3.68 (s, 3 H), 4.09 (dd, $J$ = 2.9, 5.1 Hz, 1 H), 4.44 (ddd, $J$ = 2.9, 3.7, 8.5 Hz, 1 H), 7.35 (d, $J$ = 8.3 Hz, 2 H), 7.94 (d, $J$ = 8.3 Hz, 2 H); $^{13}$C NMR (22.5 MHz, $CDCl_3$) $\delta$ 15.4, 17.1, 21.3, 31.9 (*C*HMe$_2$), 38.6 (*C*H$_2$CO$_2$-Me), 51.5 (CO$_2$*C*H$_3$), 55.6 (C$_4$), 84.0 (C$_5$), 128.0, 129.5, 134.9, 145.3, 151.1 (C$_2$), 169.3 (*C*O$_2$Me). Anal. Calcd for $C_{16}H_{21}NO_6S$: C, 54.07; H, 5.96; N, 3.94; S, 9.02. Found: C, 54.05; H, 6.03; N, 3.98; S, 9.24.

***trans*-5-*tert*-Butyl-4-[(Methoxycarbonyl)methyl]-3-tosyl-2-oxazolidinone (8g)**: mp 109.0−110.0 °C (benzene−hexane); IR (KBr disk) 1780 (s), 1740 (s) cm$^{-1}$; $^1$H NMR (60 MHz, $CDCl_3$) $\delta$ 0.86 (s, 9 H), 2.45 (s, 3 H), 2.93 (d, $J$ = 5.6 Hz, 2 H), 3.67 (s, 3 H), 4.03 (d, $J$ = 3.4 Hz, 1 H), 4.52 (dt, $J$ = 3.4, 5.6 Hz, 1 H), 7.35 (d, $J$ = 8.0 Hz, 2 H), 8.00 (d, $J$ = 8.0 Hz, 2 H). Anal. Calcd for $C_{17}H_{23}NO_6S$: C, 57.70; H, 6.37; N, 3.54. Found: C, 57.70; H, 6.28; N, 3.53.

**5,5-Dimethyl-4-[(methoxycarbonyl)methyl]-3-tosyl-2-oxazolidinone (8h)**: mp 94.5−95.5 °C (benzene−hexane); IR (KBr disk) 1775 (s), 1740 (s) cm$^{-1}$; $^1$H NMR (60 MHz, $CDCl_3$) $\delta$ 1.33 (s, 6 H), 2.45 (s, 3 H), 2.82−3.03 (m, 2 H), 3.70 (s, 3 H), 4.49 (dd, $J$ = 4.0, 8.4 Hz, 1 H), 7.33 (d, $J$ = 8.0 Hz, 2 H), 7.93 (d, $J$ = 8.0 Hz, 2 H). Anal. Calcd for $C_{15}H_{19}NO_6S$: C, 52.78; H, 5.61; N, 4.10; S, 9.39. Found: C, 52.63; H, 5.51; N, 4.18; S, 9.26.

***cis*-4-[(Methoxycarbonyl)methyl]-5-[2-(phthaloylamino)ethyl]-3-tosyl-2-oxazolidinone (8i)**: mp 201.0−201.9 °C (dichloromethane−hexane); IR (KBr disk) 1770 (s), 1730 (s), 1710 (s) cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.95 (m, 1 H), 2.05 (m, 1 H), 2.45 (s, 3 H), 2.85 (dd, $J$ = 9.2, 17.6 Hz, 1 H), 3.03 (dd, $J$ = 3.3, 17.6 Hz, 1 H), 3.66 (s, 3 H), 3.78 (dt, $J$ = 14.3, 7.3 Hz, 1 H), 3.87 (dt, $J$ = 14.3, 7.3 Hz, 1 H), 4.70 (ddd, $J$ = 3.3, 7.3, 10.3 Hz, 1 H), 4.85 (ddd, $J$ = 3.3, 7.3, 9.2 Hz, 1 H), 7.35 (d, $J$ = 8.1 Hz, 2 H), 7.73 (dd, $J$ = 3.3, 5.5 Hz, 2 H), 7.83 (dd, $J$ = 3.3, 5.5 Hz, 2 H), 7.93 (d, $J$ = 8.1 Hz, 2 H); NOE for H$_5$ (10.3%) and one of C*H*$_2$CO$_2$Me protons (3.1%) by irradiation at H$_4$; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 21.7, 28.0 (CH$_2$*C*H$_2$CH), 34.0 (*C*H$_2$CH$_2$CH), 34.7 (*C*H$_2$CO$_2$Me), 52.3 (CO$_2$*C*H$_3$), 56.6 (C$_4$), 76.4 (C$_5$), 123.3, 128.3, 128.5, 129.8, 130.0, 132.0, 134.1, 145.8, 150.9 (C$_2$), 168.0, 170.0 (*C*O$_2$Me). [*trans*-**8i**: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.95 (m, 1 H), 2.05 (m, 1 H), 2.44 (s, 3 H), 2.82 (dd, $J$ = 9.2, 17.2 Hz, 1 H), 3.22 (dd, $J$ = 3.3, 17.2 Hz, 1 H), 3.65 (s, 3 H), 3.78 (t, $J$ = 7.0 Hz, 1 H), 4.35−4.41 (m, 2 H), 7.35 (d, $J$ = 8.1 Hz, 2 H), 7.73 (dd, $J$ = 3.3, 5.5 Hz, 2 H), 7.83 (dd, $J$ = 3.3, 5.5 Hz, 2 H), 7.93 (d, $J$ = 8.1 Hz, 2 H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 21.7, 33.7 (CH$_2$*C*H$_2$-CH), 33.9 (CH$_2$CH$_2$CH), 38.3 (*C*H$_2$CO$_2$Me), 52.1 (CO$_2$*C*H$_3$), 58.2 (C$_4$), 78.3 (C$_5$), 123.3, 128.3, 128.5, 129.8, 130.0, 132.0, 134.1, 145.8, 150.9 (C$_2$), 168.0, 170.0 (*C*O$_2$Me).] Anal. Calcd for $C_{23}H_{22}N_2O_8S$: C, 56.78; H, 4.52; N, 5.76; S, 6.59. Found: C, 56.47; H, 4.52; N, 5.74; S, 6.65.

***trans*-5-Allyl-4-[(methoxycarbonyl)methyl]-3-tosyl-2-oxazolidinone (8j)**: oil; IR (neat film) 1790 (s), 1740 (s) cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 2.35−2.50 (m, 2 H), 2.46 (s, 3 H), 2.83 (dd, $J$ = 9.5, 16.9 Hz, 1 H), 3.19 (dd, $J$ = 3.3, 16.9 Hz, 1 H), 3.70 (s, 3 H), 4.37−4.42 (m, 2 H), 5.03 (dd, $J$ = 1.5, 9.0 Hz, 1 H), 5.15 (dd, $J$ = 1.5, 16.9 Hz, 1 H), 5.55 (ddt, $J$ = 9.0, 16.9, 7.0 Hz, 1 H), 7.37 (d, $J$ = 8.1 Hz, 2 H), 7.93 (d, $J$ = 8.1 Hz, 2 H); HRMS calcd for $C_{16}H_{18}NO_6S - CH_2O$ 322.0750, found *m*/*z* (relative intensity) 322.0740 ($M^+ - CH_2O$, 8.7), 312.1 (8.4), 280.1 (8.6), 198.1 (26.3), 155.0 (100.0).

***trans*-5-(1,1-Dimethylallyl)-4-[(methoxycarbonyl)methyl]-3-tosyl-2-oxazolidinone (8k)**: oil; IR (neat film) 1790 (s), 1740 (s) cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 0.98 (s, 3 H), 1.01 (s, 3 H), 2.46 (s, 3 H), 2.87 (dd, $J$ = 3.3, 16.1 Hz, 1 H), 2.95 (dd, $J$ = 6.9, 16.1 Hz, 1 H), 3.65 (s, 3 H), 4.08 (d, $J$ = 3.0 Hz, 1 H), 4.03 (dt, $J$ = 6.9, 3.3 Hz, 1 H), 4.94 (d, $J$ = 10.6 Hz, 1 H), 5.08 (d, $J$ = 17.4 Hz, 1 H), 5.52 (dd, $J$ = 10.6, 17.4 Hz, 1 H), 7.35 (d, $J$ = 8.1 Hz, 2 H), 7.93 (d, $J$ = 8.1 Hz, 2 H); HRMS calcd for $C_{18}H_{23}NO_6S$ 381.1246, found *m*/*z* (relative intensity) 381.1229 ($M^+$, 7.3), 350.1 (100.0).

***trans*-5-[2-[(Methoxycarbonyl)amino]ethyl]-4-[(methoxycarbonyl)methyl]-3-tosyl-2-oxazolidinone (8l)**: mp 108.5−109.0 °C (dichloromethane−hexane); IR (KBr disk) 3400 (m), 1785 (s), 1740 (s), 1725 (s), 1700 (s) cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.70−1.91 (m, 2 H), 2.46 (s, 3 H), 2.87 (dd, $J$ = 9.9, 17.2, 1 H), 3.17 (dd, $J$ = 2.9, 17.2 Hz, 1 H), 3.26−3.37 (m, 2 H), 3.66 (s, 3 H), 3.70 (s, 3 H), 4.36−4.39 (m, 2 H), 5.31 (br s, 1 H), 7.37 (d, $J$ = 8.1 Hz, 2 H), 7.92 (d, $J$ = 8.1 Hz, 2 H). Anal. Calcd for $C_{17}H_{22}N_2O_8S$: C, 49.27; H, 5.35; N, 6.76; S, 7.73. Found: C, 49.37; H, 5.23; N, 6.76; S, 7.60.

***trans*-4-[(Methoxycarbonyl)methyl]-5-[2-[(phenylcarbamoyl)amino]ethyl]-3-tosyl-2-oxazolidinone (8m)**: mp 109.3−109.8 °C (dichloromethane−hexane); IR (KBr disk) 3380 (w), 1780 (s), 1735 (m), 1665 (m), 1600 (m), 1555 (s) cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.69 (ddt, $J$ = 8.1, 14.3, 6.2 Hz, 1 H), 1.91 (br m, 1 H), 2.42 (s, 3 H), 2.84 (dd, $J$ = 8.8, 17.2 Hz, 1 H), 3.07 (dd, $J$ = 3.3, 17.2 Hz, 1 H), 3.26−3.36 (m, 2 H), 3.61 (s, 3 H), 4.34 (dt, $J$ = 3.3, 8.8 Hz, 1 H), 4.41 (ddd, $J$ = 3.3, 4.8,

8.1 Hz, 1 H), 5.54 (br d, $J$ = 5.9 Hz, 1 H), 7.00 (t, $J$ = 7.0 Hz, 1 H), 7.09 (br s, 1 H), 7.22−7.36 (m, 6 H), 7.90 (d, $J$ = 8.4 Hz, 2 H). Anal. Calcd for $C_{22}H_{25}N_3O_7S$: C, 55.57; H, 5.30; N, 8.84; S, 6.74. Found: C, 55.27; H, 5.19; N, 8.72; S, 6.71.

***trans*-4-[(Methoxycarbonyl)methyl]-5-[2-[(methylcarbamoyl)amino]ethyl]-3-tosyl-2-oxazolidinone (8n)**: oil; IR (neat film) 3360 (br m), 1785 (s), 1735 (s), 1650 (s), 1565 (s) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.73 (ddt, $J$ = 8.4, 14.2, 5.5 Hz, 1 H), 1.90 (tt, $J$ = 5.5, 14.2 Hz, 1 H), 2.46 (s, 3 H), 2.74 (d, $J$ = 4.8 Hz, 3 H), 2.87 (dd, $J$ = 8.8, 17.2 Hz, 1 H), 3.13 (dd, $J$ = 3.3, 17.2 Hz, 1 H), 3.27 (q, $J$ = 5.5 Hz, 2 H), 3.67 (s, 3 H), 4.39 (dt, $J$ = 8.8, 3.3 Hz, 1 H), 4.44 (ddd, $J$ = 3.3, 5.5, 8.4 Hz, 1 H), 4.80 (br q, $J$ = 4.8 Hz, 1 H), 5.10 (br t, $J$ = 5.5 Hz, 1 H), 7.37 (d, $J$ = 8.1 Hz, 2 H), 7.91 (d, $J$ = 8.1 Hz, 2 H); HRMS calcd for $C_{17}H_{23}N_3O_7S$ 413.1257, found $m/z$ (relative intensity) 413.1262 (2.2), 309.0 (100.0), 258.1 (45.8), 227.1 (63.7), 186.0 (16.8). Anal. Calcd for $C_{17}H_{23}N_3O_7S$: C, 49.38; H, 5.61; N, 10.16; S, 7.75. Found: C, 49.18; H, 5.40; N, 10.33; S, 7.65.

***trans*-4-[(Methoxycarbonyl)methyl]-3-tosyl-4-[2-(tosylamino)ethyl]-2-oxazolidinone (8o)**: mp 144.5−145.5 °C (dichloromethane−hexane); IR (KBr disk) 3540 (w), 1785 (s), 1735 (s) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.68−1.92 (m, 2 H), 2.41 (s, 3 H), 2.44 (s, 3 H), 2.80 (dd, $J$ = 9.5, 17.2 Hz, 1 H), 2.99−3.06 (m, 2 H), 3.12 (dd, $J$ = 2.9, 17.2 Hz, 1 H), 3.67 (s, 3 H), 4.34 (dt, $J$ = 2.9, 9.5 Hz, 1 H), 4.41 (ddd, $J$ = 2.9, 5.1, 8.2 Hz, 1 H), 5.21 (t, $J$ = 6.6 Hz, 1 H), 7.29 (d, $J$ = 8.1 Hz, 2 H), 7.35 (d, $J$ = 8.1 Hz, 2 H), 7.70 (d, $J$ = 8.1 Hz, 2 H), 7.90 (d, $J$ = 8.1 Hz, 2 H). Anal. Calcd for $C_{22}H_{26}N_2O_8S_2$: C, 51.76; H, 5.13; N, 5.49; S, 12.55. Found: C, 51.57; H, 5.05; N, 5.35; S, 12.73.

**2-[(Methoxycarbonyl)methyl]-1-tosylpyrrolidine (10)**: oil; IR (neat film) 1740 (s) $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 1.51−1.84 (m, 4 H), 2.43 (s, 3 H), 2.51 (dd, $J$ = 10.0, 16.0 Hz, 1 H), 3.07 (dd, $J$ = 3.7, 16.0 Hz, 1 H), 3.12 (m, 1 H), 3.46 (m, 1 H), 3.95 (m, 1 H), 7.34 (d, $J$ = 8.1 Hz, 2 H), 7.73 (d, $J$ = 8.1 Hz, 2 H); HRMS calcd for $C_{14}H_{19}NO_4S - CH_3O$: 266.0953, found $m/z$ (relative intensity) 266.0875 ($M^+ - CH_3O$, 2.0), 224.1 (53.6), 184.0 (6.0), 156.0 (3.7), 142.0 (100.0), 110.1 (11.6), 91.1 (34.9).

**4-[(Methoxycarbonyl)methyl]-3-tosyltetrahydro-1,3-oxazin-2-one (12a)**: mp 128.5−129.5 °C (benzene−hexane); IR (KBr disk) 1735 (s) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 2.15−2.29 (m, 2 H), 2.43 (s, 3 H), 2.76 (dd, $J$ = 10.6, 16.5 Hz, 1 H), 3.14 (dd, $J$ = 2.6, 16.5 Hz, 1 H), 3.73 (s, 3 H), 4.30 (dt, $J$ = 11.4, 3.7 Hz, 1 H), 4.37 (dt, $J$ = 4.0, 11.4 Hz, 1 H), 5.00 (m, 1 H), 7.32 (d, $J$ = 8.1 Hz, 2 H), 7.91 (d, $J$ = 8.1 Hz, 2 H). Anal. Calcd for $C_{14}H_{17}NO_6S$: C, 51.36; H, 5.24; N, 4.28; S, 9.79. Found: C, 51.41; H, 5.10; N, 4.21; S, 9.51.

***trans*-4-[(Methoxycarbonyl)methyl]-6-phenyl-3-tosyltetrahydro-1,3-oxazin-2-one (12b)**: mp 122.0−123.0 °C (benzene−hexane); IR (KBr disk) 1735 (s) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 2.21 (m, 1 H), 2.45 (s, 3 H), 2.48 (m, 1 H), 2.89 (dd, $J$ = 10.6, 16.1 Hz, 1 H), 3.30 (dd, $J$ = 3.3, 16.1 Hz, 1 H), 3.77 (s, 3 H), 5.04 (m, 1 H), 5.60 (dd, $J$ = 2.9, 12.1 Hz, 1 H), 7.21−7.40 (m, 7 H), 7.94 (d, $J$ = 8.4 Hz, 2 H); NOE for one of the $CH_2CO_2Me$ protons (8.5%) by irradiation at $C_6H$. Anal. Calcd for $C_{20}H_{21}NO_6S$: C, 59.54; H, 5.25; N, 3.47; S, 7.95. Found: C, 59.36; H, 5.18; N, 3.44; S, 7.98.

***trans*-6-*tert*-Butyl-4-[(methoxycarbonyl)methyl]-3-tosyltetrahydro-1,3-oxazin-2-one (12c)**: mp 142.0−143.0 °C (dichloromethane−hexane); IR (KBr disk) 1730 (s) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 0.92 (s, 9 H), 1.86 (dddd, $J$ = 1.5, 5.5, 12.5, 14.3 Hz, 1 H), 2.17 (dt, $J$ = 14.3, 2.6 Hz, 1 H), 2.43 (s, 3 H), 2.72 (dd, $J$ = 11.0, 15.8 Hz, 1 H), 3.17 (ddd, $J$ = 1.5, 3.7, 15.8 Hz, 1 H), 3.74 (s, 3 H), 4.06 (dd, $J$ = 2.6, 12.5 Hz, 1 H), 4.97 (dddd, $J$ = 2.6, 3.7, 5.5, 11.0 Hz, 1 H), 7.31 (d, $J$ = 8.1 Hz, 2 H), 7.91 (d, $J$ = 8.1 Hz, 2 H). [*cis*-**13c**: $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 0.94 (s, 9 H), 1.77 (ddd, $J$ = 9.9, 11.7, 13.6 Hz, 1 H), 2.43 (s, 3 H), 2.47 (ddd, $J$ = 1.8, 8.4, 13.6 Hz, 1 H), 2.69 (dd, $J$ = 7.7, 16.9 Hz, 1 H), 3.03 (dd, $J$ = 2.9, 16.9 Hz, 1 H), 3.73 (s, 3 H), 3.79 (dd, $J$ = 1.8, 11.7 Hz, 1 H), 4.75 (dddd, $J$ = 2.9, 7.7, 8.4, 9.9 Hz, 1 H), 7.32 (d, $J$ = 8.4 Hz, 2 H), 7.99 (d, $J$ = 8.4 Hz, 2 H).] Anal. Calcd for $C_{18}H_{25}NO_6S$: C, 56.38; H, 6.57; N, 3.65; S, 8.36. Found: C, 56.31; H, 6.43; N, 3.73; S, 8.30.

**6,6-Dimethyl-4-[(methoxycarbonyl)methyl]-3-tosyltetrahydro-1,3-oxazin-2-one (12d)**: mp 113.0−114.0 °C (benzene−hexane); IR (KBr disk) 1740 (s) $cm^{-1}$; $^1H$ NMR (60 MHz, $CDCl_3$) $\delta$ 1.38 (s, 6 H), 1.98−2.42 (m, 2 H), 2.43 (s, 3 H), 2.76−3.08 (m, 2 H), 3.65 (s, 3 H), 4.77 (m, 1 H), 7.26 (d, $J$ = 8.0 Hz, 2 H), 7.93 (d, $J$ = 8.0 Hz, 2 H). Anal. Calcd for $C_{16}H_{21}NO_6S$: C, 54.07; H, 5.96; N, 3.94; S, 9.02. Found: C, 53.93; H, 5.83; N, 3.87; S, 8.99.

**4-[(Methoxycarbonyl)methyl]-3-tosyl-3-aza-1-oxaspiro[5.5]undeca-2-one (12e)**: mp 88.5−89.5 °C (benzene−hexane); IR (KBr disk) 1730 (s) $cm^{-1}$; $^1H$ NMR (90 MHz, $CDCl_3$) $\delta$ 1.07−2.05 (m, 10 H), 1.87 (dd, $J$ = 8.8, 14.2 Hz, 1 H), 2.39 (dd, $J$ = 7.3, 14.2 Hz, 1 H), 2.43 (s, 3 H), 2.69 (dd, $J$ = 8.8, 16.5 Hz, 1 H), 3.14 (dd, $J$ = 3.4, 16.5 Hz, 1 H), 3.66 (s, 3 H), 4.79 (ddt, $J$ = 3.4, 7.3, 8.8 Hz, 1 H), 7.30 (d, $J$ = 8.5 Hz, 2 H), 7.94 (d, $J$ = 8.5 Hz, 2 H); $^{13}C$ NMR (22.5 MHz, $CDCl_3$) $\delta$ 21.3, 21.4, 24.7, 34.8, 37.8, 38.1 ($CH_2CO_2Me$), 39.8 ($C_5$), 50.5 ($C_4$), 51.4 ($CO_2CH_3$), 81.2 ($C_6$), 128.8, 128.9, 136.2, 144.6, 148.7 ($C_2$), 169.8 ($CO_2Me$). Anal. Calcd for $C_{19}H_{25}NO_6S$: C, 57.71; H, 6.37; N, 3.54; S, 8.10. Found: C, 57.92; H, 6.47; N, 3.60; S, 8.16.

***trans,cis*-4-[(Methoxycarbonyl)methyl]-5-methyl-6-phenyl-3-tosyltetrahydro-1,3-oxazin-2-one (12f)**: mp 78.5−80.5 °C (dichloromethane−hexane); IR (KBr disk) 1740 (s), 1725 (s) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 0.70 (d, $J$ = 7.0 Hz, 3 H), 2.43 (s, 3 H), 2.38 (m, 1 H), 2.96 (dd, $J$ = 11.0, 16.1 Hz, 1 H), 3.32 (dd, $J$ = 3.7, 16.1 Hz, 1 H), 3.79 (s, 3 H), 4.77 (ddd, $J$ = 1.8, 3.7, 11.0 Hz, 1 H), 5.64 (d, $J$ = 2.6 Hz, 1 H), 7.22 (d, $J$ = 8.8 Hz, 2 H), 7.26−7.35 (m, 5 H), 7.93 (d, $J$ = 8.8 Hz, 2 H); NOE for $C_5H$ (8.2%) and one of the $CH_2CO_2Me$ protons (3.1%) by irradiation at $C_6H$; HRMS calcd for $C_{21}H_{23}NO_6S$ 417.1246, found $m/z$ (relative intensity) 417 1273 ($M^+$, 6.0), 353.2 (69.8), 261.1 (18.1), 195.1 (56.2), 105.0 (51.0), 91.1 (100.0).

**4-[(Methoxycarbonyl)methyl]-3-tosyl-5,6,6-trimethyltetrahydro-1,3-oxazin-2-one (12g)**: mp 153.0−154.6 °C (benzene−hexane); IR (KBr disk) 1730 (s) $cm^{-1}$; $^1H$ NMR (60 MHz, $CDCl_3$) $\delta$ 1.06 (d, $J$ = 6.4 Hz, 3 H), 1.21 (s, 3 H), 1.35 (s, 3 H), 2.17 (m, 1 H), 2.46 (s, 3 H), 2.70−3.04 (m, 2 H), 3.47 (s, 3 H), 4.16 (ddd, $J$ = 2.6, 5.0, 9.2 Hz, 1 H), 7.20 (d, $J$ = 8.2 Hz, 2 H), 7.93 (d, $J$ = 8.2 Hz, 2 H). Anal. Calcd for $C_{17}H_{23}NO_6S$: C, 55.27; H, 6.28; N, 3.79; S, 8.68. Found: C, 54.93; H, 6.20; N, 3.75; S, 8.47.

***cis*-1-[(Methoxycarbonyl-2-methoxycarbonyl)methyl]-3-[(tosylcarbamoyl)oxy]pyrrolidine (13a)**: mp 141.5−142.0 °C (dichloromethane−hexane); IR (KBr disk) 1740 (s), 1665 (s) $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO-$d_6$, 100 °C) $\delta$ 1.73 (m, 1 H), 2.03 (m, 1 H), 2.40 (s, 3 H), 2.66 (dd, $J$ = 5.5, 17.6 Hz, 1 H), 3.14 (dd, $J$ = 8.1, 17.6 Hz, 1 H), 3.31 (m, 1 H), 3.43 (m, 1 H), 3.49 (s, 3 H), 3.60 (s, 3 H), 4.15 (dt, $J$ = 8.1, 5.5 Hz, 1 H), 5.19 (q, $J$ = 5.5 Hz, 1 H), 6.96 (br s, 1 H), 7.39 (d, $J$ = 8.1 Hz, 2 H), 7.75 (d, $J$ = 8.1 Hz, 2 H). [*trans*-**13a**: $^1H$ NMR (400 MHz, DMSO-$d_6$, 100 °C) $\delta$ 1.73 (dt, $J$ = 19.1, 6.6 Hz, 1 H), 1.91 (dt, $J$ = 19.1, 6.6 Hz, 1 H), 2.37 (s, 3 H), 2.54 (d, $J$ = 7.0 Hz, 2 H), 3.28−3.35 (m, 2 H), 3.56 (s, 3 H), 3.57 (s, 3 H), 4.05 (q, $J$ = 7.0 Hz, 1 H), 4.25 (q, $J$ = 6.6 Hz, 1 H), 6.95 (br s, 1 H), 7.32 (d, $J$ = 8.1 Hz, 2 H), 7.71 (d, $J$ = 8.1 Hz, 2 H).] Anal. Calcd for $C_{17}H_{22}N_2O_8S$: C, 49.27; H, 5.35; N, 6.76; S, 7.73. Found: C, 48.87; H, 5.20; N, 6.65; S, 7.81.

***cis*-2-[(Methoxycarbonyl)methyl]-1-(phenylcarbamoyl)-3-[(tosylcarbamoyl)oxy]pyrrolidine (13b)**: mp 138.5−140.0 °C (dichloromethane−hexane); IR (KBr disk) 3380 (m), 1740 (s), 1650 (s) $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO-$d_6$) $\delta$ 1.85 (m, 1 H), 2.11 (m, 1 H), 2.28 (dd, $J$ = 9.2, 16.1 Hz, 1 H), 2.40 (s, 3 H), 2.77 (dd, $J$ = 5.1, 16.1 Hz, 1 H), 3.36−3.54 (m, 2 H), 3.46 (s, 3 H), 4.31 (dt, $J$ = 9.2, 5.1 Hz, 1 H), 5.22 (q, $J$ = 5.1 Hz, 1 H), 6.95 (d, $J$ = 7.3 Hz, 1 H), 7.21 (br s, 1 H), 7.22 (d, $J$ = 7.3 Hz, 2 H), 7.44 (d, $J$ = 7.3 Hz, 2 H), 7.46 (d, $J$ = 8.1 Hz, 2 H), 7.79 (d, $J$ = 8.1 Hz, 2 H), 8.26 (br s, 1 H); NOE for $C_2H$ (7.9%) and one of the $C_4H_2$ methylene protons (3.8%) by irradiation at $C_3H$. Anal. Calcd for $C_{22}H_{25}N_3O_7S$: C, 55.57; H, 5.30; N, 8.84; S, 6.74. Found: C, 55.58; H, 5.26; N, 8.76; S, 6.65.

***cis*-3-Methyl-7-[(tosylcarbamoyl)oxy]-1,3-diazabicyclo[4.3.0]nonane-2,4-dione (13c):** mp 196.5−197.5 °C (dichloromethane−hexane); IR (KBr disk) 3045 (m), 1750 (s), 1720 (s), 1670 (s) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.89 (dd, $J$ =

13.2, 16.1 Hz, 1 H), 1.91 (dd, $J$ = 7.3, 13.9 Hz, 1 H), 2.35 (dd, $J$ = 3.7, 16.1 Hz, 1 H), 2.36 (s, 3 H), 2.90 (ddt, $J$ = 3.7, 13.9, 10.6 Hz, 1 H), 2.99 (s, 3 H), 3.22 (dt, $J$ = 10.6, 7.3 Hz, 1 H), 3.47 (t, $J$ = 10.6 Hz, 1 H), 3.88 (dt, $J$ = 13.2, 3.7 Hz, 1 H), 5.13 (t, $J$ = 3.7 Hz, 1 H), 7.36 (d, $J$ = 8.1 Hz, 2 H), 7.71 (d, $J$ = 8.1 Hz, 2 H); NOE for $C_6H$ (10.8%) and one of the $C_8H_2$ methylene protons (3.6%) by irradiation of the signal of $C_7H$. Anal. Calcd for $C_{16}H_{19}N_3O_6S$: C, 50.39; H, 5.02; N, 11.02; S, 8.40. Found: C, 50.32; H, 4.91; N, 10.97; S, 8.45.

***cis*-2-[(Methoxycarbonyl)methyl]-1-tosyl-3-[(tosylcarbamoyl)oxy]pyrrolidine (13d)**: mp 151.0−152.5 °C (AcOEt−hexane); IR (KBr disk) 3260 (m), 1775 (s), 1755 (s), 1745 (s) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.43 (m, 1 H), 1.76 (m, 1 H), 2.43 (s, 3 H), 2.44 (s, 3 H), 2.60 (dd, $J$ = 9.5, 16.9 Hz, 1 H), 3.03 (dd, $J$ = 4.8, 16.9 Hz, 1 H), 3.03 (dd, $J$ = 4.8, 16.9 Hz, 1 H), 3.28−3.40 (m, 2 H), 3.59 (s, 3 H), 3.95 (dt, $J$ = 9.5, 4.8 Hz, 1 H), 5.06 (br s, 1 H), 5.18 (q, $J$ = 4.8 Hz, 1 H), 7.33 (d, $J$ = 8.1 Hz, 2 H), 7.35 (d, $J$ = 8.1 Hz, 2 H), 7.70 (d, $J$ = 8.1 Hz, 2 H),7.88 (d, $J$ = 8.1 Hz, 2 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 21.6, 21.8, 31.6 ($C_4$), 39.6 ($CH_2CO_2Me$), 46.9 ($C_5$), 52.0 ($CO_2CH_3$), 76.0 ($C_3$), 128.2, 128.3, 129.8, 129.9, 133.6, 135.1, 144.4, 145.5, 148.7 (*C*ONHTs), 170.4 ($CO_2Me$). [*trans*-**13d**: $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.90 (dd, $J$ = 6.6, 14.3 Hz, 1 H), 2.08 (m, 1 H), 2.44 (dd, $J$ = 9.9, 15.8 Hz, 1 H), 2.45 (s, 3 H), 2.55 (s, 3 H), 2.88 (dd, $J$ = 4.8, 15.8 Hz, 1 H), 3.11 (ddd, $J$ = 6.7, 9.9, 11.4 Hz, 1 H), 3.56 (t, $J$ = 9.9 Hz, 1 H), 3.68 (s, 3 H), 3.93 (dd, $J$ = 4.8, 9.9 Hz, 1 H), 4.87 (d, $J$ = 3.3 Hz, 1 H), 6.55 (br s, 1 H), 7.34 (d, $J$ = 8.2 Hz, 2 H), 7.42 (d, $J$ = 8.2 Hz, 2 H), 7.61 (d, $J$ = 8.2 Hz, 2 H), 7.83 (d, $J$ = 8.2 Hz, 2 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 21.7, 21.8, 29.3 ($C_4$), 39.3 ($CH_2CO_2Me$), 46.4 ($C_5$), 52.1 ($CO_2CH_3$), 79.5 ($C_3$), 128.3, 128.4, 129.8, 129.9, 133.6, 135.1, 144.4, 145.5, 148.5 (*C*ONHTs), 170.4 ($CO_2Me$).] Anal. Calcd for $C_{22}H_{26}N_2O_8S_2$: C, 51.76; H, 5.13; N, 5.49; S, 12.55. Found: C, 51.77; H, 5.23; N, 5.30; S, 12.41.

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**Supporting Information Available:** $^1H$ NMR spectra of compounds **4**, **6**, **8d**, **8k**, **10**, and **12f** (9 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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