Palladium(II)-Promoted Cross-Coupling of 4-Alkenyl-2-azetidinones with Organomercurials[1]

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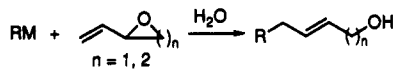
The palladium-promoted cross-coupling of 4-alkenyl-2-azetidinones with aryl and vinylic mercurials provides 5-aryl-3-alkenamides and 3,6-alkadienamides, respectively. Modest to excellent stereoselectivity for formation of the new carbon–carbon double bond is observed. The reaction becomes catalytic in palladium when cupric chloride and oxygen are introduced. This process constitutes the first organometallic ring opening of 2-azetidinones to acyclic unsaturated amides.

Introduction

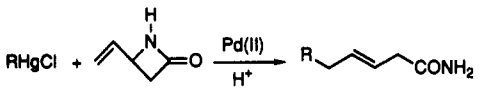
The organometallic ring opening of alkenyl epoxides[2] and oxetanes[3] has become a valuable synthetic route to allylic and homoallylic alcohols, respectively (eq 1). A



(1)

variety of organometallics, including lithium, boron, copper, and tin or mercury plus palladium, have been utilized in these reactions.

Although there are no previous reports of analogous ring-openings being effected on 4-alkenyl-2-azetidinones, we anticipated that mechanistically such processes should be possible using organomercurials and palladium reagents (eq 2). Indeed, this provides a useful new route to

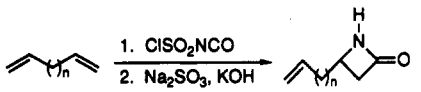


(2)

3-alkenamides, the full details of which we report here.[1]

Results and Discussion

4-Alkenyl-2-azetidinones are readily available via chlorosulfonyl isocyanate addition to conjugated or nonconjugated dienes (eq 3).[4]



(3)

We have employed procedures virtually identical to those established during our earlier work on vinylic epoxides[2d] and oxetanes[3a] to effect the cross-coupling of aryl- or vinylmercurials and 4-alkenyl-2-azetidinones. One procedure stoichiometric in palladium (procedure A: 1.0 equiv Li_2PdCl_4 and 20:1 THF/saturated aqueous NH_4Cl at 0 °C for 6–12 h and then 25 °C for 0–24 h) and one catalytic in palladium (procedure B: 10 mol % Li_2PdCl_4, 1 equiv $CuCl_2$, 1 atm O_2, and 20:1 THF/saturated aqueous NH_4Cl at 0 °C for 0–12 h and then 25 °C for 3–48 h) have been utilized to obtain modest to excellent yields of the expected 3-alkenamides. The results are summarized in Table I.

A variety of substituted 2-azetidinones with terminal or internal carbon–carbon double bonds are available from 1,3-dienes and chlorosulfonyl isocyanate,[4] and all azetidinones employed reacted with arylmercurials to afford good to excellent yields of ring-opened amide products. As expected, best results are obtained from 2-azetidinones bearing terminal double bonds (entries 1–20), but even reactions with 2-azetidinones containing internal disubstituted double bonds afford respectable yields (entries 21–26). The regioselectivity of the organopalladium addition to these carbon–carbon double bonds is apparently quite high, since we did not see any products arising from addition of the aryl group to the carbon next to the nitrogen moiety.

The stereoselectivity of these reactions is dependent on the structure of the 4-alkenyl-2-azetidinones employed. When disubstituted alkene products are formed from 2-azetidinones with terminal double bonds, the *E*-isomer is preferred in about a 3:1 ratio (entries 1 and 2). 2-Azetidinones with internal double bonds give almost exclusively the *E*-disubstituted product (entries 21–26). Alkenamides containing trisubstituted double bonds can be obtained from arylmercurials in excellent yields using both stoichiometric and catalytic procedures (entries 4–12), but there is no stereoselectivity in the formation of these trisubstituted alkenes. On the other hand, vinylmercurials afford 3,6-alkadienamides bearing new trisubstituted carbon–carbon double bonds with stereoselectivities of 2:1 to 4:1 when the stoichiometric procedure A is employed (entries 13 and 15). Both the yields and stereoselectivities drop when the catalytic procedure B is utilized (entries 14 and 16). Tetrasubstituted alkene products can also be formed from these reactions and reasonable stereoselectivity has been observed using the catalytic procedure, although the yield is low (entries 19 and 20). The stereochemical assignment for this tetrasubstituted alkene have been established by NOESY spectroscopy.

Arylmercurials other than phenylmercuric chloride have also been examined. Both electron-donating and electron-withdrawing groups on the aryl ring are readily accommodated in these reactions and give comparable yields and stereoselectivities (entries 6–12).

Vinylmercurials tend to give significantly lower yields

(1) For a preliminary communication see: Larock, R. C.; Ding, S. *Tetrahedron Lett.* **1989**, *30*, 1897.

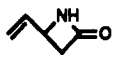
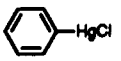
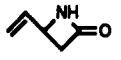
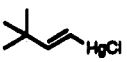
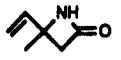
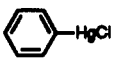
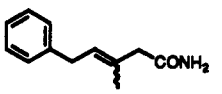
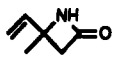
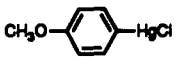
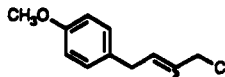
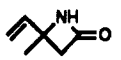
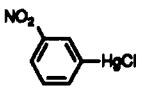
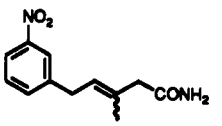
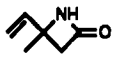
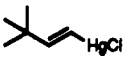
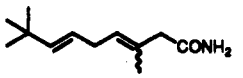
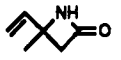
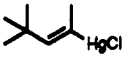
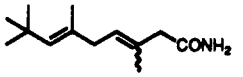
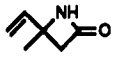
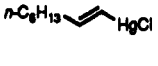
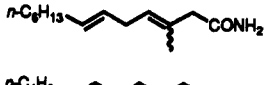
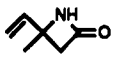
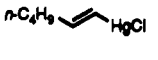
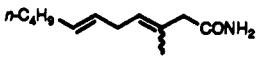
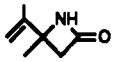
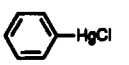
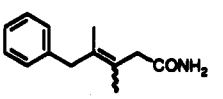
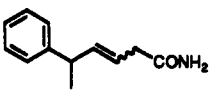
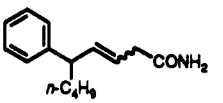
(2) (a) Larock, R. C. *Comprehensive Organic Transformations*; VCH Publishers: New York, 1989; p 123. (b) Echavarren, A. M.; Tueting, D. R.; Stille, J. K. *J. Am. Chem. Soc.* **1988**, *110*, 4039. (c) Tueting, D. R.; Echavarren, A. M.; Stille, J. K. *Tetrahedron* **1989**, *45*, 979. (d) Larock, R. C.; Ilkka, S. J. *Tetrahedron Lett.* **1986**, *27*, 2211.

(3) (a) Larock, R. C.; Stolz-Dunn, S. K. *Tetahedron Lett.* **1988**, *29*, 5069. (b) Larock, R. C.; Stolz-Dunn, S. K. *Synlett* **1990**, 341.

(4) (a) Durst, T.; O'Sullivan, M. J. *J. Org. Chem.* **1970**, *35*, 2043. (b) Moriconi, E. J.; Meyer, W. C. *Tetrahedron Lett.* **1968**, 3823. (c) Moriconi, E. J.; Meyer, W. C. *J. Org. Chem.* **1971**, *36*, 2841.

0022-3263/93/1958-2081$04.00/0

Table I. Palladium-Promoted Reaction of 4-Alkenyl-2-azetidinones and Organomercuric Chlorides

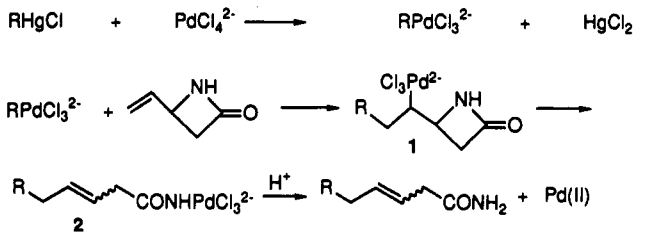
entry	2-azetidinone	RHgCl	procedure[a]	reaction conditions	product	E/Z ratio	% isolated yield
1			A	0 °C, 11 h; 25 °C, 3 h		74:26	60
2[b]			B	0 °C, 3 h; 25 °C, 24 h		72:28	57
3			A	0 °C, 11 h; 25 °C, 3 h		-	0
4			A	0 °C, 11 h; 25 °C, 3 h		52:48	90
5			B	0 °C, 2 h; 25 °C, 10 h		49:51	91
6			A	0 °C, 10 h; 25 °C, 6 h		47:53	73
7[c]			A	0 °C, 6 h		44:56	77
8			B	0 °C, 12 h; 25 °C, 3 h		50:50	74
9			A	0 °C, 8 h; 25 °C, 7 h		54:46	56
10[c]			A	0 °C, 6 h		53:47	79
11			B	0 °C, 2 h; 25 °C, 7 h		53:47	32
12[d]			B	25 °C, 8 h		48:52	52
13			A	0 °C, 12 h; 25 °C, 3 h		81:19	34
14			B	0 °C, 2 h; 25 °C, 9 h		59:41	18
15			A	0 °C, 11 h; 25 °C, 5 h		68:32	54
16			B	0 °C, 2 h; 25 °C, 8 h		51:49	35
17			A	0 °C, 10 h; 25 °C, 24 h		-	0
18			B	25 °C, 48 h		-	0
19			A	0 °C, 12 h; 25 °C, 2 h		52:48	85
20			B	0 °C, 3 h; 25 °C, 15 h		83:17	41
21			A	0 °C, 10 h; 25 °C, 8 h		90:10	51
22			B	0 °C, 2 h; 25 °C, 9 h		95:5	32
23[e]			B	0 °C, 1 h; 25 °C, 8 h		100:0	38
24			A	0 °C, 10 h; 25 °C, 8 h		95:5	55
25			B	0 °C, 3 h; 25 °C, 18 h		100:0	26
26[e]			B	0 °C, 1 h; 25 °C, 8 h		100:0	42

[a] See the text and the Experimental Section for an explanation of the procedures. [b] One equivalent of 2-azetidinone was used. [c] Five percent H_2O was used instead of aqueous NH_4Cl. [d] No NH_4Cl or H_2O was added. [e] Two equivalents of $CuCl_2$ were used.

than arylmercurials. Like the corresponding vinylmercurial reactions with epoxides[2d] and oxetanes,[3a] the more sterically hindered the vinylmercurial, the higher the yield of amide product (compare entries 3 and 15–17). No products have even been observed when *E*-3,3-dimethyl-1-butenylmercuric chloride (entry 3), *E*-1-hexenylmercuric chloride (entry 18) and *E*-1-octenylmercuric chloride (entry 17) were employed. In general, lower yields were obtained when the catalytic procedure was employed with vinylmercurials. The difficulties are presumably due to the easy dimerization of the less hindered vinylmercurials to 1,3-dienes.[5]

A possible mechanism for the palladium(II)-promoted cross-coupling of 4-alkenyl-2-azetidinones with organomercurials is shown in Scheme I. While no experiments have been run to attempt to support (or disprove) this mechanism, analogous mechanisms have been proposed to explain the reactions of vinylic epoxides[2d] or oxetanes[3a] with organomercurials in the presence of a palladium(II) salt.

Scheme I

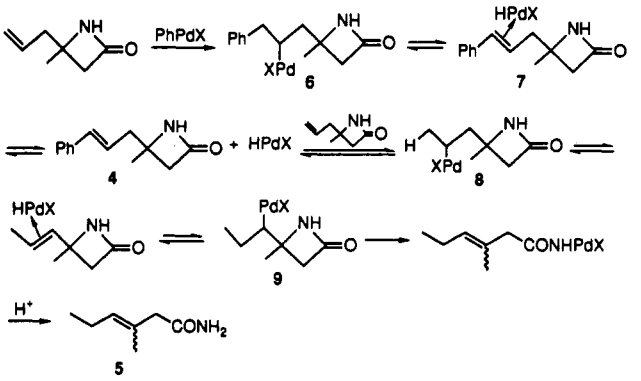


The first step of the mechanism involves transmetallation of the organomercurial by the palladium(II) salt. The organopalladium species then adds to the double bond of the 4-alkenyl-2-azetidinone to form σ-alkylpalladium species 1. The organic ligand adds to the least hindered end of the carbon–carbon double bond or the carbon more remote from the nitrogen. This σ-alkylpalladium species then undergoes palladium amide elimination to form species 2. The water or ammonium chloride in the system then protonates this species to form the amide product and regenerates palladium(II).

The mechanism shown in Scheme I indicates that the reaction between 4-alkenyl-2-azetidinones and organo-

(5) (a) Larock, R. C. *J. Org. Chem.* **1976**, *41*, 2241. (b) Larock, R. C.; Riefling, B. *J. Org. Chem.* **1978**, *43*, 1468.

Scheme II

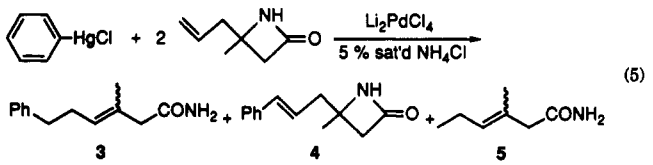


mercurials should be catalytic with respect to palladium(II). Our earlier work with vinylic epoxides[2d] indicated that such a process might not be very efficient. Apparently, the palladium(II) can be reduced to palladium(0) during the course of this type of reaction or in some other way be removed from the catalytic cycle. This type of process can, however, be made quite efficient by introducing copper(II) salts to reoxidize the palladium, and oxygen to reoxidize copper(I) to copper(II) (eq 4). Indeed, this

$$\mathrm{Pd(0)} + 2\,\mathrm{Cu(II)} \longrightarrow \mathrm{Pd(II)} + 2\,\mathrm{Cu(I)} \xrightarrow{O_2} 2\,\mathrm{Cu(II)} \qquad (4)$$

approach works quite well for the synthesis of 3-alkenamides and nearly as well in most cases as the reaction stoichiometric in palladium. Little change in the stereochemistry of the alkenamide product is usually observed in these catalytic reactions.

We have previously taken advantage of the ability of palladium to migrate down carbon chains and subsequently ring open epoxides.[6] We have examined such a possibility in our azetidinone chemistry. 4-Allyl-4-methyl-2-azetidinone, in which the carbon–carbon double bond and the 2-azetidinone ring are separated by one carbon, has been allowed to react with phenylmercuric chloride using either the stoichiometric or catalytic procedure (eq 5). None of



(5)

the desired 3-alkenamide **3** was observed using either procedure. In the presence of a stoichiometric amount of Pd(II) salt (procedure A: 0 °C, 12 h; 25 °C, 3 h), 64 and 57% yields of compounds **4** (*E* only) and **5** (*E*/*Z* = 45:55), respectively, were obtained. None of the expected products **3**–**5** were observed when the catalytic procedure was employed.

A mechanism is shown in Scheme II which explains how the β-hydride eliminated product **4** and the hydride product **5** are formed in this reaction (eq 5). Product **4** is formed by a Heck reaction[7] with the apparent driving force being benzylic hydride elimination and formation of the disubstituted, conjugated C–C double bond of intermediate **7** and product **4**. The resulting palladium hydride species proceeds to react with the less hindered C–C double bond of the starting azetidinone present in excess to produce the expected ring-opened unsaturated amide **5**. In this case, the initial adduct **8** can either reversibly generate the starting azetidinone and HPdX or migrate palladium to form an intermediate **9** which proceeds to ring-opened amide **5**. The latter process apparently wins out due to the irreversible nature of the ring-opening step and the inability to form prior stabilized conjugated C–C double bond products. Finally, if the addition of the palladium hydride species to the double bond of the starting azetidinone is quantitative, equal amounts of products **4** and **5** should be obtained, and this is indeed observed.

Conclusion

The palladium-promoted cross-coupling of 4-alkenyl-2-azetidinones with arylmercurials provides a high yielding route to 5-aryl-3-alkenamides. The reaction of vinylmercurials generally affords lower yields of the ring-opened 3,6-alkadienamides than that of arylmercurials. Like the corresponding oxetane reactions,[3a] but unlike the reactions of the corresponding vinylic epoxides,[2d] these reactions exhibit only modest stereoselectivity. The 3-alkenamides are generally isolated as mixtures of *E*- and *Z*-isomers, except when a disubstituted carbon–carbon double bond bearing large organic substituents is generated. Then the *E*-isomer is formed almost exclusively. Catalytic amounts of palladium can be employed in the reaction if cupric chloride and oxygen are used to reoxidize the palladium. These are the first observed examples of 4-alkenyl-2-azetidinones reacting with organometallic reagents to afford 3-alkenamides.

Experimental Section

General Procedures. The proton and carbon nuclear magnetic resonance spectra were recorded at 300 MHz for hydrogen nuclei and 75.5 MHz for carbon nuclei. Elemental analyses were performed by Galbraith Laboratories, Inc.

Reagents. All reagents were used directly as obtained commercially unless noted otherwise. Palladium chloride was donated by Johnson Matthey, Inc. and Kawaken Fine Chemicals Co., Ltd. Tetrahydrofuran (THF) and ethyl ether were distilled from CaH_2 and stored over molecular sieves. Chlorosulfonyl isocyanate was purchased from Aldrich Chemical Co., Inc. and used without further purification. 1,3-Butadiene, 2-methyl-1,3-butadiene, and 2,3-dimethyl-1,3-butadiene were obtained from Aldrich Chemical Co., Inc. (*E*)- and (*Z*)-1,3-Pentadiene, (*E*)- and (*Z*)-1,3-octadiene, and 2-methyl-1,4-pentadiene were purchased from Wiley Organics.

Organomercurials. Phenylmercuric chloride was used as purchased from Fluka. The other arylmercurials used were prepared by simple electrophilic mercuration of the corresponding arene.[8] The vinylmercurials used were synthesized using a hydroboration–mercuration procedure.[9]

General Procedure for the Preparation of 4-Alkenyl-2-azetidinones. The 4-alkenyl-2-azetidinones were prepared by the reaction of the corresponding dienes and chlorosulfonyl isocyanate according to the literature procedures.[4] The diene (10 mmol) was added dropwise to a stirred solution of chlorosulfonyl isocyanate (10 mmol) in 6 mL of distilled ether at −10 to 0 °C. After maintaining the reaction temperature at 0 °C for an additional hour, the solution was added slowly to a stirred

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mixture of 25 mL of 25% aqueous Na_2SO_3 and 10 mL of ether. The aqueous phase was kept slightly basic by adding 10% KOH solution as the reduction proceeded. After 30 min, the layers were separated and the aqueous layer was successively extracted with three 20-mL portions of ether. The combined ether extracts were dried by anhydrous Na_2SO_4, filtered, and evaporated. The crude product was purified by flash column chromatography to give the corresponding 4-alkenyl-2-azetidinone as a colorless oil.

4-Vinyl-2-azetidinone, (*E*)- and (*Z*)-4-(1-propenyl)-2-azetidinone (38:62 *E*/*Z*), 4-methyl-4-vinyl-2-azetidinone and 4-isopropenyl-4-methyl-2-azetidinone were prepared by the procedure of Moriconi and Meyer and exhibited spectroscopic data identical to that reported earlier.[4c]

(*E*)-4-(1-Hexenyl)-2-azetidinone. Obtained in 25% isolated yield from the reaction of a mixture of (*E*)- and (*Z*)-1,3-hexadiene and chlorosulfonyl isocyanate: ^{1}H NMR ($CDCl_3$) δ 0.86 (t, 3 H, J = 7.0 Hz, CH_3), 1.29 (m, 4 H, $CH_2CH_2CH_3$), 1.99 (m, 2 H, CH_2Pr), 2.64 (ddd, 1 H, J = 15.0 Hz, J = 2.3 Hz, J = 1.4 Hz, CHCO cis to hexenyl), 3.14 (ddd, 1 H, J = 15.0 Hz, J = 5.2 Hz, J = 2.0 Hz, CHCO trans to hexenyl), 4.08 (m, 1 H, CHN), 5.45 (ddt, 1 H, J = 15.3 Hz, J = 7.6 Hz, J = 1.2 Hz, C*H*=CHBu), 5.70 (dt, 1 H, J = 15.3 Hz, J = 6.8 Hz, =CHBu), 6.28 (br s, 1 H, NH); IR (neat) 3261 (NH), 1767 (C=O), 1670 (C=C) cm^{-1}.

4-Allyl-4-methyl-2-azetidinone. Obtained in 54% isolated yield from the reaction of 2-methyl-1,4-pentadiene and chlorosulfonyl isocyanate: ^{1}H NMR ($CDCl_3$) δ 1.40 (s, 3 H, CH_3), 2.39 (m, 2 H, CH_2C=), 2.64 (dd, 1 H, J = 14.6 Hz, J = 1.7 Hz, CHCO trans or cis to methyl), 2.78 (dd, 1 H, J = 14.6 Hz, J = 1.6 Hz, CHCO cis or trans to methyl), 5.13 (d, 1 H, J = 17.5 Hz, =CH_2 cis to methylene), 5.14 (d, 1 H, J = 10.0 Hz, =CH_2 trans to methylene), 5.76 (m, 1 H, C*H*=CH_2), 6.15 (br s, 1 H, NH); IR (neat) 3225 (NH), 1726 (C=O), 1643 (C=C) cm^{-1}; HRMS: calcd for $C_7H_{12}NO$ (M + H) m/z 126.09189, found 126.09177.

General Stoichiometric Procedure for the Palladium-Promoted Cross-Coupling of 4-Alkenyl-2-Azetidinones with Organomercurials (Procedure A). The following procedure used for the preparation of a mixture of (*E*)- and (*Z*)-3-methyl-5-phenyl-3-pentenamide is representative of that used for other compounds. A solution of $PdCl_2$ (88 mg, 0.5 mmol), anhydrous LiCl (42 mg, 0.5 mmol), and distilled THF (12 mL) was allowed to stir under N_2 at room temperature for 4–6 h. To this solution at 0 °C was added sequentially saturated aqueous NH_4Cl (0.6 mL), 2 equiv of 4-methyl-4-vinyl-2-azetidinone (111 mg, 1.0 mmol), and 1 equiv of PhHgCl (157 mg, 0.5 mmol). The solution mixture was allowed to stir under N_2 at 0 °C for 11 h and then at room temperature for 3 h. Ether (15 mL) was then added to the reaction mixture. The ether layer was washed with saturated aqueous NH_4Cl (15 mL × 2), and the combined aqueous layers were back-extracted with ether (15 mL × 2). The combined ether fractions were dried over $MgSO_4$. After removal of the solvents, the residue was purified by flash column chromatography on silica gel using hexane and ethyl acetate as eluants. (*E*)- and (*Z*)-3-Methyl-5-phenyl-3-pentenamide were obtained in 90% yield (52:48 *E*/*Z*) as a white solid.

General Catalytic Procedure for the Palladium-Promoted Cross-Coupling of 4-Alkenyl-2-azetidinones with Organomercurials (Procedure B). The following catalytic procedure used for the preparation of a mixture of (*E*)- and (*Z*)-3-methyl-5-phenyl-3-pentenamide is representative of that used for other compounds. A solution of $PdCl_2$ (8.8 mg, 0.05 mmol), anhydrous LiCl (4.2 mg, 0.05 mmol), anhydrous $CuCl_2$ (67 mg, 1.0 mmol), and distilled THF (12 mL) was allowed to stir under N_2 at room temperature for 4–6 h. To this solution at 0 °C was added sequentially saturated aqueous NH_4Cl (0.6 mL), 2 equiv of 4-methyl-4-vinyl-2-azetidinone (111 mg, 1.0 mmol), and 1 equiv of PhHgCl (157 mg, 0.5 mmol). The reaction flask was flushed with O_2. The solution was allowed to stir at 0 °C for 2 h and then at room temperature for 10 h. Ether (15 mL) was then added to the reaction mixture. The ether layer was washed with saturated aqueous NH_4Cl (15 mL × 2), and the combined aqueous layers were back-extracted with ether (15 mL × 2). The combined ether fractions were dried over $MgSO_4$. After removal of the solvent, the residue was purified by flash column chromatography on silica gel using hexane and ethyl acetate as eluants. (*E*)- and (*Z*)-3-Methyl-5-phenyl-3-pentenamide were obtained in 91% yield (49:51 *E*/*Z*) as a white solid.

The stereochemistry of all *E*/*Z* mixtures of alkenamides was determined by integration of the 300 MHz ^{1}H NMR spectral peaks corresponding to the allylic hydrogens next to the amide group.

The purity of the alkenamide products have been established by elemental analysis or ^{1}H and ^{13}C NMR spectroscopy (see the supplemental material).

(*E*)- and (*Z*)-5-Phenyl-3-pentenamide (Table I, entry 1). *E*-Isomer: ^{1}H NMR ($CDCl_3$) δ 2.97 (d, 2 H, J = 7.1 Hz, CH_2CO), 3.38 (d, 2 H, J = 6.6 Hz, CH_2Ph), 5.40–6.00 (m, 4 H, CH=CH, NH_2), 7.10–7.40 (m, 5 H, phenyl); ^{13}C NMR ($CDCl_3$) δ 33.5, 38.9, 123.9, 126.1, 128.4, 128.4, 134.5, 139.8, 173.7.

***Z*-Isomer:** ^{1}H NMR ($CDCl_3$) same as the *E*-isomer or not seen, except δ 3.14 (d, 2 H, J = 7.5 Hz, CH_2CO); ^{13}C NMR same as the *E*-isomer or not seen, except δ 34.6, 39.8, 122.6, 128.2, 128.5, 132.8.

The following spectral data were taken from a mixture of the *E*- and *Z*-isomers: mp 76–78 °C; IR (neat) 3362 (NH), 1713 (C=O) cm^{-1}; HRMS: calcd for $C_{11}H_{13}NO$ m/z 175.09972, found 175.09995.

(*E*)- and (*Z*)-3-Methyl-5-phenyl-3-pentenamide (Table I, entry 4). *E*-Isomer: ^{1}H NMR ($CDCl_3$) δ 1.83 (s, 3 H, CH_3), 2.97 (s, 2 H, CH_2CO), 3.41 (d, 2 H, J = 7.3 Hz, CH_2Ph), 5.40–5.68 (br s, 2 H, NH_2), 5.57 (t, 1 H, J = 7.3 Hz, =CH), 7.10–7.30 (m, 5 H, phenyl); ^{13}C NMR ($CDCl_3$) δ 16.2, 34.4, 47.2, 125.9, 128.1, 128.4, 128.7, 130.8, 140.6, 173.7.

***Z*-Isomer:** ^{1}H NMR ($CDCl_3$) same as the *E*-isomer or not seen, except δ 3.11 (s, 2 H, CH_2CO), 3.39 (d, 2 H, J = 7.0 Hz, CH_2Ph), 5.64 (t, 1 H, J = 7.0 Hz, CH=); ^{13}C NMR same as the *E*-isomer or not seen, except δ 25.4, 39.3.

The following spectral data were taken from a mixture of the *E*- and *Z*-isomers: mp 87–88 °C; IR (neat) 3375 (NH), 1653 (C=O) cm^{-1}; HRMS: calcd for $C_{12}H_{15}NO$ m/z 189.11537, found 189.11556.

(*E*)- and (*Z*)-3-Methyl-5-(4-methoxyphenyl)-3-pentenamide (Table I, entry 7). *E*-Isomer: ^{1}H NMR ($CDCl_3$) δ 1.81 (s, 3 H, CCH_3), 2.95 (s, 2 H, CH_2CO), 3.34 (d, 2 H, J = 7.2 Hz, CH_2Ar), 3.77 (s, 3 H, OCH_3), 5.53 (t, 1 H, J = 7.2 Hz, CH=), 5.72 and 6.15 (2 br s, 2 H, NH_2), 6.83 (d, 2 H, J = 8.7 Hz, H's on C3 and C5 of aryl), 7.07 (d, 2 H, J = 8.7 Hz, H's on C2 and C6 of aryl); ^{13}C NMR ($CDCl_3$) δ 16.1, 33.3, 47.2, 55.1, 113.9, 128.4, 129.1, 130.4, 132.6, 157.8, 173.9.

***Z*-Isomer:** ^{1}H NMR ($CDCl_3$) same as the *E*-isomer or not seen, except δ 1.83 (s, 3 H, CH_3), 3.08 (s, 2 H, CH_2CO), 5.62 (t, 1 H, J = 7.0 Hz, CH=); ^{13}C NMR same as the *E*-isomer or not seen, except δ 23.9, 39.4, 129.0, 130.1, 132.4, 157.8, 173.1.

The following spectral data were taken from a mixture of the *E*- and *Z*-isomers: mp 111–112 °C; IR (neat) 3362 (NH), 1661 (C=O) cm^{-1}; HRMS: calcd for $C_{13}H_{17}NO_2$ m/z 219.12593, found 219.12577. Anal. calcd for $C_{13}H_{17}NO_2$: C, 71.21, H, 7.81, N, 6.39. Found: C, 71.48, H, 7.78, N, 6.43.

(*E*)- and (*Z*)-3-Methyl-5-(3-nitrophenyl)-3-pentenamide (Table I, entry 10). *E*-Isomer: ^{1}H NMR ($CDCl_3$) δ 1.81 (s, 3 H, CH_3), 2.98 (s, 2 H, CH_2CO), 3.50 (d, 2 H, J = 7.2 Hz, CH_2Ar), 5.53 (t, 1 H, J = 7.2 Hz, CH=), 5.65 and 5.85 (2 br s, 2 H, NH_2), 7.43 (d, 1 H, J = 7.5 Hz, H on C6 of aryl), 7.49 (dd, 1 H, J = 7.8 Hz, J = 7.5 Hz, H on C5 of aryl), 8.01 (s, 1 H, H on C2 of aryl), 8.03 (d, 1 H, J = 7.8 Hz, H on C4 of aryl); ^{13}C NMR ($CDCl_3$) δ 16.2, 33.8, 47.2, 121.1, 123.1, 126.5, 129.3, 131.9, 134.5, 142.5, 148.4, 172.6.

***Z*-Isomer:** ^{1}H NMR ($CDCl_3$) same as the *E*-isomer or not seen, except δ 1.84 (s, 3 H, CH_3), 3.07 (s, 2 H, CH_2CO), 5.56 (t, 1 H, J = 7.2 Hz, CH=); ^{13}C NMR same as the *E*-isomer or not seen, except δ 24.1, 34.0, 39.3, 121.1, 123.0, 126.3, 129.3, 132.6, 134.5, 173.3.

The following spectral data were taken from a mixture of the *E*- and *Z*-isomers: mp 97.5–98.5 °C; IR (neat) 3379 (NH), 1632 (C=O) cm^{-1}; HRMS: calcd for $C_{12}H_{14}N_2O_3$ m/z 234.10045, found 234.10056.

(*E*,*E*)- and (*Z*,*E*)-3,8,8-Trimethyl-3,6-nonadienamide (Table I, entry 13). *E*,*E*-Isomer: ^{1}H NMR ($CDCl_3$) δ 0.99 (s, 9 H, $(CH_3)_3C$), 1.69 (s, 3 H, CH_3C=), 2.73 (t, 2 H, J = 6.6 Hz, CH_2-CH=), 2.93 (s, 2 H, CH_2CO), 5.25 (dt, 1 H, J = 15.6 Hz, J = 6.6 Hz, C*H*=CH-*t*-Bu), 5.34 (t, 1 H, J = 6.6 Hz, C*H*=CCH_3), 5.45 (d, 1 H, J = 15.6 Hz, =CH-*t*-Bu), 5.68 (br s, 2 H, NH_2); ^{13}C NMR ($CDCl_3$) δ 16.2, 29.7, 31.4, 32.9, 47.4, 122.1, 128.9, 130.4, 142.4, 173.9.

***Z,E*-Isomer**: ^{1}H NMR ($CDCl_3$) same as the *E,E*-isomer or not seen, except δ 1.79 (s, 3 H, CH_3C=), 2.99 (s, 2 H, CH_2CO); ^{13}C NMR same as the *E,E*-isomer or not seen.

The following spectral data were taken from a mixture of the *E,E*- and *Z,E*-isomers: mp 112–114 °C; IR (neat) 3371 (NH), 1728 (C=O) cm^{-1}; HRMS: calcd for $C_{12}H_{21}NO$ *m/z* 195.16232, found 195.16251.

(*E,E*)- and (*Z,E*)-3,6,8,8-Tetramethyl-3,6-nonadienamide (Table I, entry 15). *E,E*-Isomer: ^{1}H NMR ($CDCl_3$) δ 1.08 (s, 9 H, $(CH_3)_3C$), 1.68 and 1.70 (2 s, 6 H, 2 CH_3C=), 2.66 (d, 2 H, J = 7.2 Hz, CH_2CH=), 2.94 (s, 2 H, CH_2CO), 5.17 (s, 1 H, =CH-*t*-Bu), 5.35 (t, 1 H, J = 7.2 Hz, =$CHCH_2$), 5.53 and 5.67 (2 br s, 2 H, NH_2); ^{13}C NMR ($CDCl_3$) δ 16.2, 17.3, 31.1, 32.1, 40.3, 47.6, 125.6, 129.1, 132.3, 135.9, 173.6.

***Z,E*-Isomer**: ^{1}H NMR ($CDCl_3$) same as the *E,E*-isomer or not seen, except δ 1.80 (s, 3 H, CH_3CCH_2CO), 2.64 (d, 2 H, J = 7.2 Hz, CH_2CH=), 3.00 (s, 2 H, CH_2CO), 5.45 (t, 1 H, J = 7.2 Hz, =$CHCH_2$); ^{13}C NMR same as the *E,E*-isomer or not seen, except δ 17.4, 24.0, 31.1, 40.2, 173.1.

The following spectral data were taken from a mixture of the *E,E*- and *Z,E*-isomers: mp 80 °C dec; IR (neat) 3377 (NH), 1744 (C=O) cm^{-1}; HRMS: calcd for $C_{13}H_{23}NO$ *m/z* 209.17797, found 209.17815.

(*E*)- and (*Z*)-3,4-Dimethyl-5-phenyl-3-pentenamide (Table I, entry 19). *E*-Isomer: ^{1}H NMR ($CDCl_3$) δ 1.67 (s, 3 H, CH_3-CCCO), 1.90 (s, 3 H, CH_3CCPh), 3.09 (s, 2 H, CH_2CO), 3.48 (s, 2 H, CH_2Ph), 5.70 (br s, 2 H, NH_2), 7.10–7.35 (m, 5 H, phenyl); ^{13}C NMR ($CDCl_3$) δ 18.6, 19.5, 40.2, 42.2, 124.5, 126.0, 128.2, 123.4, 132.5, 140.0, 173.6.

***Z*-Isomer**: ^{1}H NMR ($CDCl_3$) same as the *E*-isomer or not seen, except δ 1.71 (s, 3 H, CH_3CCPh), 1.82 (s, 3 H, CH_3CCCO), 3.14 (s, 2 H, CH_2CO), 3.44 (s, 2 H, CH_2Ph); ^{13}C NMR same as the *E*-isomer or not seen.

The following spectral data were taken from a mixture of the *E*- and *Z*-isomers: mp 98–99 °C; IR (neat) 3369 (NH), 1661 (C=O) cm^{-1}; HRMS: calcd for $C_{13}H_{17}NO$ *m/z* 203.13102, found 203.13126.

(*E*)- and (*Z*)-5-Phenyl-3-hexenamide (Table I, entry 21). *E*-Isomer: ^{1}H NMR ($CDCl_3$) δ 1.37 (d, 3 H, J = 7.2 Hz, CH_3), 2.96 (d, 2 H, J = 6.9 Hz, CH_2CO), 3.49 (p, 1 H, J = 6.9 Hz, CHPh), 5.58 (ddt, 1 H, J = 15.5 Hz, J = 6.9 Hz, J = 1.2 Hz, $CHCH_2CO$), 5.81 (ddt, 1 H, J = 15.5 Hz, J = 6.9 Hz, J = 1.2 Hz, $CHCHPh$), 5.67 and 6.17 (2 br s, 2 H, NH_2), 7.15–7.32 (m, 5 H, phenyl); ^{13}C NMR ($CDCl_3$) δ 21.0, 39.8, 42.2, 121.9, 126.2, 127.0, 128.4, 140.5, 145.2, 174.0.

***Z*-Isomer**: ^{1}H NMR ($CDCl_3$) same as the *E*-isomer or not seen, except δ 3.17 (d, 2 H, J = 7.5 Hz, CH_2CO); ^{13}C NMR same as the *E*-isomer or not seen, except δ 23.1, 35.6, 119.2.

The following spectral data were taken from a mixture of the *E*- and *Z*-isomers: mp 59–61 °C; IR (neat) 3356 (NH), 1664 (C=O) cm^{-1}; HRMS: calcd for $C_{12}H_{15}NO$ *m/z* 189.11537, found 189.11503.

(*E*)-5-Phenyl-3-nonenamide (Table I, entry 26). ^{1}H NMR ($CDCl_3$) δ 0.86 (t, 3 H, J = 7.0 Hz, CH_3), 1.20–1.35 (m, 4 H, $CH_2CH_2CH_3$), 1.71 (q, 2 H, J = 7.8 Hz, CH_2Pr), 2.96 (d, 2 H, J = 6.9 Hz, CH_2CO), 3.25 (q, 1 H, J = 7.8 Hz, CHPh), 5.56 (ddt, 1 H, J = 15.6 Hz, J = 6.9 Hz, J = 0.9 Hz, $CHCH_2CO$), 5.78 (dd, J = 15.6 Hz, J = 7.8 Hz, $CHCHPh$), 5.51–5.82 (2 br s, 2 H, NH_2), 7.13–7.34 (m, 5 H, phenyl); ^{13}C NMR ($CDCl_3$) δ 14.0, 22.6, 29.8, 35.4, 39.9, 48.8, 122.1, 126.2, 127.4, 128.5, 140.2, 144.4, 173.7; IR (neat) 3333 (NH), 1744 (C=O) cm^{-1}; HRMS: calcd for $C_{15}H_{21}NO$ *m/z* 231.16232, found 231.16258.

(*E*)-4-Methyl-4-(3-phenyl-2-propenyl)-2-azetidinone (4) and (*E*)- and (*Z*)-3-Methyl-3-hexenamide (5) (eq 5). The ratio of the inseparable mixture of compounds **4** and **5** and the *E*- to *Z*-isomer ratio of compound **5** were determined by integration of the 300-MHz ^{1}H NMR spectral peaks corresponding to the allylic hydrogens next to the amide group.

Compound 4: ^{1}H NMR ($CDCl_3$) δ 1.49 (s, 3 H, CH_3), 2.56 (d, 2 H, J = 7.8 Hz, CH_2C=), 2.70 and 2.84 (2 d, 2 H, J = 15.0 Hz, CH_2CO), 6.13–6.23 (br s, 1 H, NH), 6.18 (dt, 1 H, J = 15.6 Hz, J = 7.8 Hz, CH=CHPh), 6.49 (d, 1 H, J = 15.6 Hz, =CHPh), 7.15–7.35 (m, 5 H, phenyl).

***E*-Isomer of compound 5**: ^{1}H NMR ($CDCl_3$) δ 0.97 (t, 3 H, J = 7.5 Hz, CH_3CH_2), 1.68 (s, 3 H, CH_3C=), 2.06 (p, 2 H, J = 7.5 Hz, CH_2CH_3), 2.91 (s, 2 H, CH_2CO), 5.36 (t, 1 H, J = 7.5 Hz, CH=), 5.55 and 5.85 (br s, 2 H, NH_2).

***Z*-Isomer of compound 5**: ^{1}H NMR ($CDCl_3$) same as the *E*-isomer of compound C or not seen except δ 1.77 (s, 3 H, CH_3C=), 2.03 (p, 2 H, J = 7.5 Hz, CH_2CH_3), 2.99 (s, 2 H, CH_2CO), 5.41 (t, 1 H, J = 7.5 Hz, CH=).

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Supplementary Material Available: ^{1}H and/or ^{13}C NMR spectra for all alkenamides without an elemental analysis (14 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.