investigation. We are grateful to ICR Research Associates for running the MS samples.

Registry No. **1a**·HCl, 21911-75-1; **1a** (ethyl ester), 21911-74-0; **1b**·HCl, 21911-78-4; **1b** (ethyl ester), 21911-77-3; **1c**·HCl, 120547-25-3; **1c** (ethyl ester), 120547-24-2; (±)-**2a**, 120547-17-3; (±)-**2b**, 120662-11-5; (±)-**2c**, 120547-26-4; (±)-**3a**, 120547-18-4; (±)-**3b**, 120547-27-5; (±)-**3c**, 120547-28-6; (±)-**4b**, 120577-47-1; (±)-**5a**, 120547-19-5; (±)-**5b**, 120547-29-7; (±)-**5c**, 120547-30-0; (±)-**6b**, 120547-20-8; DL-**7**·HCl, 120547-21-9; **8**, 120547-22-0; **9b**, 87732-27-2; **9c**, 120547-31-1; (±)-**10b**, 120547-23-1; (±)-**10c**, 120662-12-6; TsCl, 98-59-9; $C_6H_5NH_2$, 62-53-3; (±)-$MeCHBrCO_2Et$, 41978-69-2; cyclopentadiene, 542-97-2; cyclooctene, 931-88-4; cycloheptene, 628-92-2.

Cycloadditions of (Alkylarylamino)ketenes with Imines. *cis*-3-Amino-2-azetidinones

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The in situ cycloaddition of (alkylarylamino)ketenes with various imines to form predominately *cis*-3-amino-2-azetidinones is described. A mechanism involving a dipolar intermediate is provided whereby the structure of the intermediate is determined by both electronic and steric effects.

The discovery of β-lactam antibiotics has stimulated a lot of interest in the synthesis of β-lactams and their derivatives.[1] The synthesis of *cis*-3-amino-2-azetidinones continues to be a very active research area because of the importance of this structural unit in penicillin and related antibiotics.[2] It has been reported that reactions of azidoacetyl chloride or phthaloylglycyl chloride and imines in the presence of triethylamine form β-lactams, which may be converted to 3-amino-2-azetidinones.[3] More recently, several improved methods for the synthesis of 3-amino β-lactams have been reported by the treatment of azidoacetic acid, phthaloylglycine, or a Dane salt of glycine and an imine with a reagent for activating the carbonyl group in the presence of triethylamine.[2b,c,4] Some of these methods offer a stereocontrolled synthesis of cis 3-amino β-lactams. In the course of our work on the chemistry of ketenes, we demonstrated the intermediacy of (alkylarylamino)ketene in the reaction of *N*-alkyl-*N*-arylglycine and cycloalkenes in the presence of triethylamine. Since the cycloaddition of a ketene and an imine is one of the most important methods for the synthesis of β-lactams,[5] we investigated the reactions of (alkylarylamino)ketenes and imines and studied the stereochemistry of the resulting 3-amino β-lactams. We report here the results of this study.

An *N*-alkyl-*N*-arylglycine hydrochloride was stirred with 1 equiv of an imine, 1 equiv of *p*-toluenesulfonyl chloride, and 4–5 equiv of triethylamine in benzene at room temperature for 8–10 h. The corresponding β-lactams were obtained in moderate to good yield (Scheme I). Imines with various substituents in the benzene rings were pre-

Scheme I

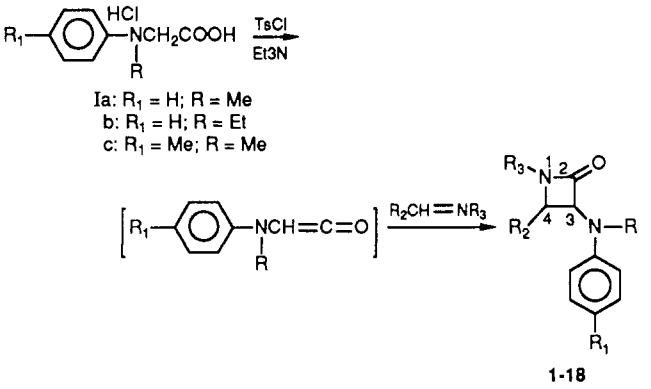
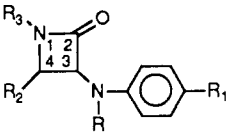


Table I. 3-(Alkylarylamino)-2-azetidinones



compd	R	R_1	R_2	R_3	isomer	yield, %
1	Me	H	C_6H_5	C_6H_5	cis	64
2	Et	H	C_6H_5	C_6H_5	cis	70
3	Me	Me	C_6H_5	C_6H_5	cis	63
4	Me	H	-CH=CHC_6H_5	C_6H_5	cis	71
5	Me	Me	-CH=CHC_6H_5	C_6H_5	cis	57
6	Et	H	*p*-ClC_6H_4	C_6H_5	cis	61
7	Me	H	*p*-Cl-C_6H_4	C_6H_5	cis	53
8	Me	H	C_6H_5	*tert*-butyl	cis	68
9	Et	H	C_6H_5	*tert*-butyl	cis	47
10	Et	H	*p*-$MeOC_6H_4$	*p*-$MeOC_6H_4$	cis	73
11	Me	H	*p*-$MeOC_6H_4$	*p*-$MeOC_6H_4$	cis	68
12	Me	H	C_6H_5	*p*-$MeOC_6H_4$	cis	70
13	Et	H	*o*-$NO_2C_6H_4$	C_6H_4	cis	68
14	Me	H	*o*-$NO_2C_6H_4$	C_6H_5	cis	62
15	Me	H	*p*-$NO_2C_6H_4$	*p*-$MeOC_6H_4$	cis	72
16a	Me	H	*o*-$MeOC_6H_4$	C_6H_5	cis	53
16b	Me	H	*o*-$MeOC_6H_4$	C_6H_5	trans	8
17a	Et	H	*o*-$MeOC_6H_4$	C_6H_5	cis	46
17b	Et	H	*o*-$MeOC_6H_4$	C_6H_5	trans	8
18a	Et	H	*p*-$MeOC_6H_4$	*p*-$NO_2C_6H_4$	cis	59
18b	Et	H	*p*-$MeOC_6H_4$	*p*-$NO_2C_6H_4$	trans	20

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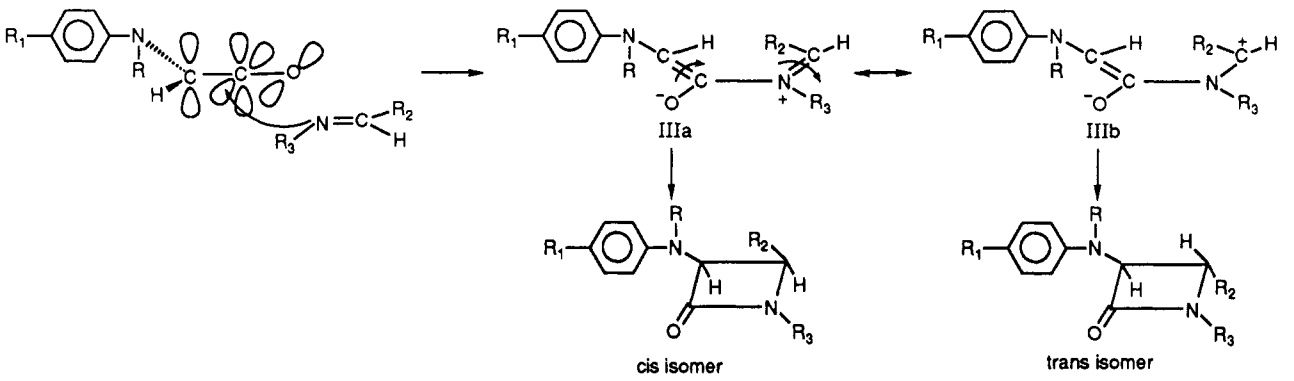
0022-3263/89/1954-2838$01.50/0

Scheme II



pared and used in this study as illustrated in Table I. The structures of the β-lactams were determined by IR, MS, and ^1H and ^{13}C NMR spectra. In most cases, Attached Proton Test (APT) NMR experiments were performed to distinguish the different carbons. The stereochemistry at C_3 and C_4 of the β-lactam rings was established by ^1H NMR analysis. The cis isomer gives a larger coupling constant (J_{cis} = 5 Hz) than the trans isomer (J_{trans} = 2 Hz).[6] All the β-lactams prepared in this study (except **16b**, **17b**, **18b**) were the cis isomers on the basis of the ^1H NMR data. To determine if the trans isomer were the result of isomerization, the corresponding cis isomers were subjected to the reaction conditions for 8–10 h. No evidence of the trans isomer could be found in any of the three control experiments. The trans isomer **16b** was treated under the reaction conditions overnight and no isomerization to the cis isomer was observed.

The above-described results may be satisfactorily explained by the reaction of the glycine derivatives with *p*-toluenesulfonyl chloride to form a mixed anhydride. This mixed anhydride can eliminate *p*-toluenesulfonic acid in the presence of triethylamine to yield the aminoketene, which has been trapped by us with cycloalkenes.[7] Molecular orbital studies suggest that electrophilic attack on ketene will occur from above the plane of the ketene skeleton, while nucleophilic attack will occur in the plane of ketene.[8] The nucleophilic attack of the nonbonding electrons of the nitrogen atom of the imine on ketene would involve reaction with the LUMO of the ketene (IIa).

The substituents on the ketene are expected to determine the preferred direction of attack. The approach of the imine nitrogen should be from the least hindered side in the plane of the ketene on the LUMO.[9] It is the p lobe on the sp-hybridized carbon of the aminoketene anti to the large amino group that is expected to interact with the lone-pair electrons of nitrogen in the imine.[10] Since the trans conformation of the imine is preferred, the above approach will give the zwitterionic intermediate IIIa (Scheme II). This dipolar intermediate may be represented by several different resonance structures. Structure IIIa would be expected to be a major contribution to the resonance hybrid of the dipolar intermediate and a conrotatory ring closure of IIIa results in the β-lactams with cis conformation. When both R_2 and R^3 are cation-stabilizing groups (**1** to **12**) or R^2 is a cation-destabilizing group (**13** to **15**), the resonance contribution of IIIa should be significantly more stabilized by these substituents and result in only cis isomers of the β-lactam. When R_2 is a better cation-stabilizing group than R_3 (**16** to **18**), resonance structure IIIb should make more of a contribution to the dipolar intermediate. Thus, the thermodynamically controlled ring closure of IIIb results in the formation of the trans isomer, which has been shown to be the more stable isomer by epimerization studies.[11]

The dehydrohalogenation of acid halides by triethylamine is a reliable method to generate ketenes. However, it has been reported that the stereochemistry of β-lactams formed by the reaction of acid halides with imines in the presence of triethylamine is hard to predict. Generally, the β-lactams formed from the reactions between chloroacetyl chloride, phenylacetyl chloride, thioacetyl chloride, or phthaloylacetyl chloride with an imine in the presence of triethylamine are the trans isomers, while the cis and trans β-lactams result from azidoacetyl chloride or alkoxyacetyl chloride. When azidoacetyl chloride reacts with the C=N bond of a thiazoline or thiazine, only the trans isomer was obtained.[12] Also, only the trans isomer was obtained when ketenes react with alkyl *N*-phenylformimidates, PhN=CHOR.[12,13] We believe these results can be explained by the mechanism described above. If the substituent on the ketene is a good carbanion-stabilizing group, resonance structure IVb of the dipolar intermediate could be expected to be a major contribution to the resonance hybrid. The more thermodynamically stable trans isomer should be formed predominately when structure IVb is the major contributor. It is well-known that chlorine, sulfur, phenyl, and phthaloyl[14] are good carbanion-stabilizing groups, thus the trans β-lactams are expected to be observed. The alkoxy and azido substituents provide much less stabilization of the carbanion[15] and both cis and

(6) (a) Nelson, D. A. *Tetrahedron Lett.* **1971**, 2543. (b) Decazes, J.; Luche, J. L.; Kagan, H. B. *Tetrahedron Lett.* **1970**, 3661.
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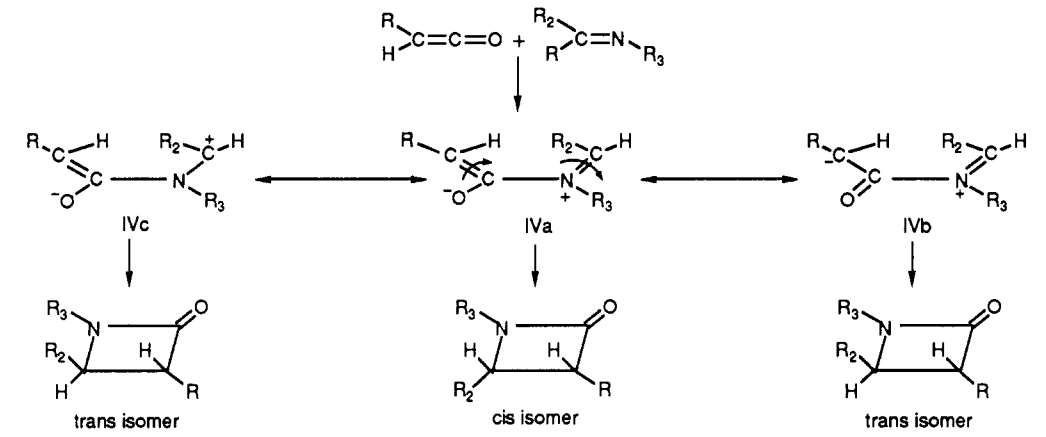
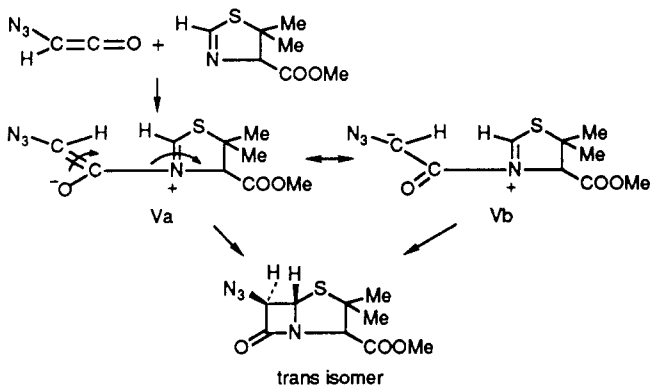
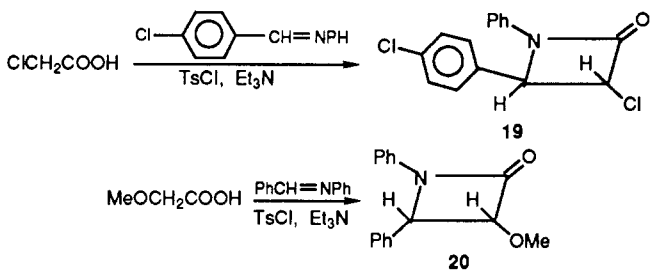
Scheme III



Scheme IV



Scheme V



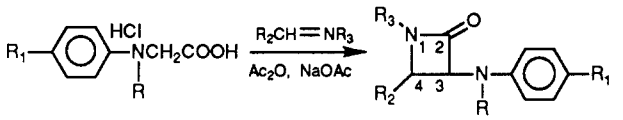
trans isomers are expected. If R_2 is a good cation-stabilizing group, such as alkoxy, IVc would be a major contributor to the resonance hybrid and the trans isomer would be expected (Scheme III).

When the configuration of the imine is locked in the cisoid conformation, such as with thiazoline, either resonance structure Va or Vb of the dipolar intermediate will result in the trans isomer (Scheme IV).

To further test the above-described model, we treated chloroacetic acid and methoxyacetic acid with *p*-toluenesulfonyl chloride and an imine in the presence of an excess of triethylamine (Scheme V). The trans β-lactam **19** was obtained in 28% yield from chloroacetic acid and the cis β-lactam was obtained in 52% yield from methoxyacetic acid. A considerable amount of black tar was observed in the chloroacetic acid reaction, which was probably the result of polymerization of chloroketene and accounts for the low yield of the trans β-lactam. These stereochemical results are consistent with those from the dehydrohalogenation of acid halides by triethylamine, which suggests that these reactions occur via a ketene pathway.

We and others have observed the presence of ketene intermediates in the reaction of substituted acetic acids with acetic anhydride and sodium acetate.[16] Therefore we treated some *N*-alkyl-*N*-arylglycine hydrochlorides and imines with acetic anhydride and sodium acetate (Table II). The resulting β-lactams were obtained in low to modest yield with predictable stereochemistry on the basis of the above discussion. This method provides an alternative route to the β-lactams but the yields are somewhat lower.

Table II. 3-(Alkylarylamino)-2-azetidinone Prepared by the Acetic Anhydride–Sodium Acetate Method



19a: R = Me; R_1 = H
b: R = Et; R_1 = H
c: R = Me; R_1 = Me

compd	R	R_1	R_2	R_3	isomer	yield, %
8	Me	H	C_6H_5	*tert*-butyl	cis	23[a]
8	Me	H	C_6H_5	*tert*-butyl	cis	45
16a	Me	H	*o*-$MeOC_6H_4$	C_6H_5	cis	trace
16b	Me	H	*o*-$MeOC_6H_4$	C_6H_5	trans	39
21	Me	Me	*p*-$NO_2C_6H_4$	*p*-$MeOC_6H_4$	cis	26

[a] Reaction was run in refluxing benzene.

In conclusion, the structure of the dipolar intermediate that is formed in the reaction of a ketene and an imine is determined by both electronic and steric consideration as described above. The stereochemistry of the resulting β-lactams depends on the structure of the dipolar intermediate.

Experimental Section

NMR spectra were recorded on a VXR-300 spectrometer, employing deuteriochloroform as the solvent with TMS as the internal standard. Attached Proton Test (APT) NMR experiments were performed to distinguish different carbons. The IR spectra were obtained on a Perkin-Elmer Model 1330 spectrometer. Column chromatography was performed on Florisil, 100–200 mesh. Rotary preparative chromatography was performed with silica gel 60PF254 from EM Science Co. Benzene and triethylamine were dried by sodium and freshly distilled before use. All melting points are uncorrected.

Imines were prepared by general procedures and *N*-alkyl-*N*-arylglycine hydrochlorides were prepared by procedures described previously.[7]

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General Procedure for the Preparation of β-Lactams. An *N*-alkyl-*N*-arylglycine hydrochloride was stirred with 1 equiv of *p*-toluenesulfonyl chloride, 1 equiv of an imine, and 4–5 equiv of triethylamine in benzene at room temperature. The reactions were conducted under a nitrogen atmosphere and in flame-dried glassware by using a magnetic stirrer. After 8 to 10 h, cold 5% aqueous NaOH solution was added to the reaction mixture. The organic layer was separated and the aqueous layer was extracted with benzene and combined with the organic layer. The benzene solution was washed with water and dried over anhydrous magnesium sulfate. After filtration and evaporation of the solvent, the concentrated solution was subjected to the florisil column chromatography using 3% EtOAc–hexane to 15% EtOAc–hexane as eluting solvent. In most cases, a crystalline product was obtained after the evaporation of eluting solvent. Analytical samples were obtained by recrystalization or rotary thin-layer preparative chromatography.

***cis*-1,4-Diphenyl-3-(methylphenylamino)-2-azetidinone (1).** From 1 g of Ia and 0.9 g of the *N*-phenylimine of benzaldehyde, 1.5 g (64%) of compound 1 was obtained: mp 180–182 °C; IR 1735, 1605, 1510 cm^{-1}; ^1H NMR ($CDCl_3$) 7.5–6.6 (m, 15 H), 5.48 (d, 1 H, J = 5.1 Hz), 5.42 (d, 1 H, J = 5.1 Hz), 2.6 (s, 3 H); ^{13}C NMR (APT) 164.2 (C), 147.9 (C) 137.7 (C)8, 134.1 (C), 129.4 (CH), 129.1 (CH), 128.4 (CH), 127.9 (CH), 127.0 (CH), 124.5 (CH), 117.8 (CH), 117.4 (CH), 112.2 (CH), 70.9 (CH), 62.3 (CH), 35.6 (CH_3); MS (relative intensity) 329 (M^+ + 1, 35.5), 328 (M, 10.1), 182 (12.2), 118 (100).

Anal. Calcd for $C_{22}H_{20}N_2O$: N, 8.53. Found: N, 8.51.

***cis*-1,4-Diphenyl-3-(ethylphenylamino)-2-azetidinone (2).** From 1.1 g of Ib and 0.93 g of the *N*-phenylimine of benzaldehyde 1.2 g (70%) of compound 2 was obtained: mp 149–150 °C; IR 1735, 1605, 1510 cm^{-1}; ^1H NMR ($CDCl_3$) 7.5–6.8 (m, 15 H), 5.46 (d, 1 H, J = 5.1 Hz), 5.42 (d, 1 H, J = 5.1 Hz), 3.4 (m, 1 H), 2.95 (m, 1 H), 0.9 (t, 3 H); ^{13}C NMR (APT) 164.2 (C), 146.7 (C), 137.8 (C), 134.2 (C), 129.2 (CH), 129.1 (CH), 128.4 (CH), 127.9 (CH), 127.2 (CH), 124.4 (CH), 117.7 (CH), 117.4 (CH), 113.0 (CH), 71.6 (CH), 62.6 (CH), 43.6 (CH_2), 13.1 (CH_3); MS (relative intensity) 343 (M^+ + 1, 100), 342 (M^+, 96.7), 182 (15.4).

***cis*-1,4-Diphenyl-3-(*p*-tolylmethylamino)-2-azetidinone (3).** From 1.8 g of Ic and 1.5 g of the *N*-phenylimine of benzaldehyde was obtained 1.8 g (63%) of compound 3: mp 207–208 °C; IR 1735, 1605, 1510 cm^{-1}; ^1H NMR ($CDCl_3$) 7.6–7.1 (m, 10 H), 7.1 (d, 2 H), 6.6 (d, 2 H), 5.46 (d, 1 H, J = 5.1 Hz), 5.42 (d, 1 H, J = 5.1 Hz), 2.6 (s, 3 H), 2.3 (s, 3 H); ^{13}C NMR 164.3, 145.9, 134.3, 130.2, 130.0, 129.5, 129.1, 128.4, 127.9, 127.0, 124.4, 117.4, 112.5, 71.2, 62.5, 45.8, 35.6; MS (relative intensity) 343 (M^+ + 1, 100), 342 (M^+, 32.5) 132 (91.5).

Anal. Calcd for $C_{23}H_{22}N_2O$: N, 8.19. Found: N, 8.11.

***cis*-1-Phenyl-3-(methylphenylamino)-4-(2-phenylethenyl)-2-azetidinone (4).** From 1.5 g of Ia and 1.5 g of the *N*-phenylimine of cinnamaldehyde was obtained 1.9 (71%) of compound 4: mp 125–127 °C; IR 1730, 1600, 1500 cm^{-1}; ^1H NMR ($CDCl_3$) 7.6–6.6 (m, 16 H), 6.2 (dd, 1 H, J = 16 Hz, 7.5 Hz), 5.3 (d, 1 H, J = 4.8 Hz), 5.0 (dd, 1 H, J = 7.5 Hz, 4.8 Hz), 3.2 (s, 3 H); ^{13}C NMR (APT) 163.7 (C), 148.4 (C), 137.9 (C), 135.8 (C), 135.1 (CH), 129.2 (CH), 128.6 (CH), 128.1 (CH), 126.5 (CH), 124.5 (CH), 123.2 (CH), 118.1 (CH), 117.2 (CH), 112.7 (CH), 112.6 (CH), 70.7 (CH), 61.6 (CH), 36.3 (CH_3).

Anal. Calcd for $C_{24}H_{22}N_2O$: C, 81.35; H, 6.21; N, 7.91. Found: C, 81.19; H, 6.11; N, 7.83.

***cis*-1-Phenyl-3-(*p*-tolylmethylamino)-4-(2-phenylethenyl)-2-azetidinone (5).** From 2.15 g of Ic and 2.07 g of the *N*-phenylimine of cinnamaldehyde, 2.1 g (57%) of compound 5 was obtained: mp 194–195 °C; IR 1730, 1600, 1500 cm^{-1}; ^1H NMR ($CDCl_3$) 7.5–6.5 (m, 15 H), 6.1 (dd, 1 H, J = 16 Hz, 7.5 Hz), 5.2 (d, 1 H, J = 4.8 Hz), 4.9 (dd, 1 H, J = 7.5 Hz, 4.8 Hz), 3.1 (s, 3 H), 2.1 (s, 3 H); ^{13}C NMR (APT) 164.2 (C), 146.3 (C), 137.9 (C) 135.9 (C), 134.9 (CH), 129.7 (CH), 129.2 (CH), 128.6 (CH)8 128.1 (CH), 127.4 (CH), 126.5 (CH), 123.4 (CH), 123.3 (CH), 117.2 (CH), 112.9 (CH), 71.0 (CH), 61.8 (CH), 36.5 (CH_3), 20.3 (CH_3).

Anal. Calcd for $C_{25}H_{24}N_2O$: N, 7.61. Found: N, 7.46.

***cis*-1-Phenyl-3-(ethylphenylamino)-4-(*p*-chlorophenyl)-2-azetidinone (6).** From 2.15 g of Ib and 2.15 g of the *N*-phenylimine of *p*-chlorobenzaldehyde, 2 g (53%) of compound 6 was obtained: mp 149–150 °C; ^1H NMR ($CDCl_3$) 7.5–6.6 (m, 14 H), 5.43 (d, 1 H, J = 5.1 Hz), 5.37 (d, 1 H, J = 5.1 Hz), 3.3 (m, 1 H), 3.0 (m, 1 H), 1.0 (t, 3 H); ^{13}C NMR 163.8, 146.5, 137.4, 133.8, 132.8, 129.7, 129.3, 129.1, 128.6, 124.5, 117.9, 117.2, 113.0, 71.4, 61.9, 43.7, 13.2.

Anal. Calcd for $C_{23}H_{21}N_2ClO$: C, 73.33; H, 5.57; N, 7.43. Found: C, 73.38; H, 5.50; N, 7.40.

***cis*-1-Phenyl-3-(methylphenylamino)-4-(*p*-chlorophenyl)-2-azetidinone (7).** From 1.5 g of Ia and 1.6 g of the *N*-phenylimine of *p*-chlorobenzaldehyde, 1.7 g (61%) of compound 7 was obtained: mp 157–160 °C; ^1H NMR ($CDCl_3$) 7.5–6.7 (m, 14 H), 5.5 (d, 1 H, J = 5.1 Hz)8 5.4 (d, 1 H, J = 5.1 Hz), 2.7 (s, 3 H); ^{13}C NMR (APT) 163.8 (C), 147.4 (C), 137.4 (C), 133.9 (C), 132.8 (C), 129.3 (CH), 129.2 (CH), 128.7 (CH), 128.4 (CH), 124.7 (CH), 118.0 (CH), 117.3 (CH), 112.3 (CH), 71.0 (CH), 61.8 (CH), 35.7 (CH_3).

Anal. Calcd for $C_{22}H_{19}N_{20}Cl$: C, 72.83; H, 5.24; N, 7.72. Found: C, 72.67; H, 5.34; N, 7.66.

***cis*-1-*tert*-Butyl-*cis*-3-(methylphenylamino)-4-phenyl-2-azetidinone (8).** From 2 g of Ia and 1.6 g of the *N*-*tert*-butylimine of benzaldehyde, 2.1 g (68%) of compound 8 was obtained: mp 139–140 °C; IR 1735, 1600, 1510 cm^{-1}; ^1H NMR ($CDCl_3$) 7.3–7.3 (m, 7 H), 6.7–6.5 (m, 3 H), 5.08 (d, 1 H, J = 4.8 Hz), 5.01 (d, 1 H, J = 4.8 Hz), 2.9 (s, 9 H); ^{13}C NMR 166.2, 147.7, 136.7, 128.7, 128.1, 127.8, 127.5, 117.1, 111.8, 70.2, 62.7, 54.5, 35.9, 28.1; MS (relative intensity) 309 (M^+ + 1, 100), 308 (M^+, 10.6), 209 (18), 162 (17), 118 (92).

***cis*-1-*tert*-Butyl-3-(ethylphenylamino)-4-phenyl-2-azetidinone (9).** From 2.15 g of Ib and 1.6 g of the *N*-*tert*-butylimine of benzaldehyde, 1.5 g (47%) of an oily compound was obtained: IR 1735, 1600, 1510 cm^{-1}; ^1H NMR ($CDCl_3$) 7.0–6.1 (m, 10 H), 4.61 (d, 1 H, J = 4.8 Hz), 4.57 (d, 1 H, J = 4.8 Hz), 3.2 (m, 1 H), 2.8 (m, 1 H), 1.0 (s, 9 H), 0.9 (t, 3 H); ^{13}C NMR 165.9, 146.3, 136.6, 129.1, 128.7, 128.5, 127.5, 116.8, 112.4, 70.0, 62.5, 54.3, 43.7, 27.9, 13.1; MS (relative intensity) 323 (M^+ + 1, 2.9), 276 (1.6), 178 (4.4).

***cis*-1,4-Bis(*p*-methoxyphenyl)-3-(ethylphenylamino)-2-azetidinone (10).** From 1.8 g of Ib and 2.0 g of the *N*-(*p*-methoxyphenyl)imine of *p*-methoxybenzaldehyde, 2.3 g (68%) of compound 10 was obtained: mp 125–127 °C; IR 1730, 1610, 1530 cm^{-1}; ^1H NMR ($CDCl_3$) 7.4–6.6 (m, 13 H), 5.37 (d, 1 H, J = 5.0 Hz), 5.32 (d, 1 H, J = 5.0 Hz), 3.8 (s, 3 H), 3.7 (s, 3 H), 3.4 (m, 1 H), 3.0 (m, 1 H), 1.0 (t, 3 H); ^{13}C NMR (APT) 163.5 (C), 159.2 (C), 156.3 (C), 146.7 (C), 131.3 (C), 129.0 (CH), 128.4 (CH), 126.1 (C), 118.6 (CH), 117.5 (CH), 114.4 (CH), 113.8 (CH), 112.8 (CH), 71.3 (CH), 62.3 (CH), 55.5 (CH_3), 55.2 (CH_3), 43.7 (CH_2), 13.2 (CH_3).

Anal. Calcd for $C_{25}H_{26}N_2O_3$: C, 74.62; H, 6.47; N, 6.96. Found: C, 74.52; H, 6.55; N, 6.92.

***cis*-1,4-Bis(*p*-methoxyphenyl)-3-(methylphenylamino)-2-azetidinone (11).** From 1.5 g of Ia and 1.8 g of the *N*-(*p*-methoxyphenyl)imine of *p*-methoxybenzaldehyde, 2.1 g (73%) of compound 11 was obtained: mp 150–153 °C; IR 1730, 1610, 1530 cm^{-1}; ^1H NMR ($CDCl_3$) 7.4–6.6 (m, 13 H), 5.42 (d, 1 H, J = 4.8 Hz), 5.35 (d, 1 H, J = 4.8 Hz), 3.8 (s, 3 H), 3.7 (s, 3 H), 2.8 (s, 3 H); ^{13}C NMR 163.5, 159.3, 156.3, 147.9, 131.3, 129.0, 128.2, 126.0, 118.7, 117.6, 114.4, 113.8, 112.2, 70.8, 62.1, 55.5, 55.1, 35.7.

Anal. Calcd for $C_{24}H_{24}N_2O_3$: C, 74.23; H, 6.18; N, 7.21. Found: C, 73.98; H, 6.10; N, 7.21.

***cis*-1-(*p*-Methoxyphenyl)-3-(methylphenylamino)-4-phenyl-2-azetidinone (12).** From 1.5 g of Ia and 1.6 g of the *N*-(*p*-methoxyphenyl)imine of benzaldehyde, 1.85 g (70%) of compound 12 was obtained: mp 160–163 °C; IR 1735, 1610, 1520 cm^{-1}; ^1H NMR nCDCl$_3$) 7.4–6.6 (m, 14 H), 5.47 (d, 1 H, J = 4.8 Hz), 5.40 (d, 1 H, J = 4.8 Hz), 3.8 (s, 3 H), 2.7 (s, 3 H); ^{13}C NMR 164.0, 156.4, 147.9, 134.2, 131.3, 129.0, 128.3, 127.9, 127.0, 118.6, 117.7, 114.4, 112.2, 70.9, 62.4, 55.4, 35.6.

Anal. Calcd for $C_{23}H_{22}N_2O_2$: C, 77.09; H, 6.14; N, 7.82. Found: C, 76.87; H, 5.97; N, 7.76.

***cis*-1-Phenyl-3-(ethylphenylamino)-4-(*o*-nitrophenyl)-2-azetidinone (13).** From 1.5 g of Ib and 1.6 g of the *N*-phenylimine of *o*-nitrobenzaldehyde, 1.9 g (68%) of compound 13 was obtained: mp 170–172 °C; IR 1740, 1600, 1510 cm^{-1}; ^1H NMR ($CDCl_3$) 8.2–6.8 (m, 14 H), 6.3 (d, 1 H, J = 5.4 Hz), 5.6 (d, 1 H, J = 5.4 Hz), 3.2 (m, 1 H), 2.8 (m, 1 H), 0.7 (t, 3 H); ^{13}C NMR (APT) 165.6 (C), 148.1 (C), 146.4 (C), 137.7 (C), 133.7 (C), 131.6 (CH), 129.4 (CH), 129.2 (CH), 129.0 (CH), 128.8 (CH), 125.7 (CH), 124.7 (CH), 119.8 (CH), 117.2 (CH), 116.3 (CH), 73.8 (CH), 60.9 (CH), 43.7 (CH_2), 12.5 (CH_3).

Anal. Calcd for $C_{23}H_{21}N_3O_3$: C, 71.32; H, 5.42; N, 10.85. Found: C, 71.20; H, 5.37; N, 10.81.

***cis*-1-Phenyl-3-(methylphenylamino)-4-(*o*-nitrophenyl)-2-azetidinone (14).** From 2 g of Ia and 2.26 g of the *N*-phenylimine of *o*-nitrobenzaldehyde, 2.3 g (62%) of compound **14** was obtained: mp 202–203 °C; IR 1740, 1600, 1510 cm^{-1}; ^1H NMR ($CDCl_3$) 8.2–6.8 (m, 14 H), 6.3 (d, 1 H, J = 5.4 Hz), 5.7 (d, 1 H, J = 5.4 Hz), 2.4 (s, 3 H); ^{13}C NMR (APT) 165.3 (C), 148.3 (C), 148.0 (C), 137.9 (C), 134.0 (CH), 131.8 (C), 129.8 (CH), 129.5 (CH), 129.4 (CH), 129.3 (CH), 126.1 (CH), 125.1 (CH), 119.4 (CH), 117.5 (CH), 113.7 (CH), 72.8 (CH), 61.3 (CH), 35.9 (CH_3).

Anal. Calcd for $C_{22}H_{19}N_3O_3$: C, 70.77; H, 5.09; N, 11.26. Found: C, 70.69; H, 4.98; N, 11.23.

***cis*-1-(*p*-Methoxyphenyl)-3-(methylphenylamino)-4-(*p*-nitrophenyl)-2-azetidinone (15).** From 1.5 g of Ia and 1.9 g of the *N*-(*p*-methoxyphenyl)imine of *p*-nitrobenzaldehyde, 2.15 g (72%) of compound **15** was obtained: mp 135–137 °C; IR 1745, 1600, 1520 cm^{-1}; ^1H NMR ($CDCl_3$) 7.9–6.5 (m, 13 H), 5.52 (d, 1 H, J = 4.8 Hz), 5.46 (d, 1 H, J = 4.8 Hz), 3.8 (s, 3 H), 2.7 (s, 3 H); ^{13}C NMR (APT) 162.0 (C), 156.6 (C), 147.6 (C), 147.2 (C), 142.2 (C), 130.7 (C), 129.5 (CH), 129.1 (CH), 127.8 (CH), 123.3 (CH), 118.2 (CH), 114.4 (CH), 112.1 (CH), 71.4 (CH), 61.8 (CH), 55.3 (CH_3), 35.5 (CH_3).

Anal. Calcd for $C_{23}H_{21}N_3O_4$: C, 68.48; H, 5.21; N, 10.42. Found: C, 68.29; H, 5.22; N, 10.36.

***cis*-1-Phenyl-3-(methylphenylamino)-4-(*o*-methoxyphenyl)-2-azetidinone (16a) and *trans*-1-Phenyl-3-(methylphenylamino)-4-(*o*-methoxyphenyl)-2-azetidinone (16b).** From 2 g of Ia and 2.1 g of the *N*-phenylimine of *o*-methoxybenzaldehyde, 1.9 g (53%) of **16a** and 0.3 g (8%) of **16b** were obtained. The separation of the two isomers was achieved by rotary chromatography and the cis isomer has a larger R_f value than the trans isomer.

16a: mp 143–145 °C; IR 1740, 1590, 1490 cm^{-1}; ^1H NMR ($CDCl_3$) 7.6–6.6 (m, 14 H), 5.6 (d, 1 H, J = 4.8 Hz), 5.5 (d, 1 H, J = 4.8 Hz), 3.1 (s, 3 H), 2.7 (s, 3 H); ^{13}C NMR (APT) 165.0 (C), 157.1 (C), 148.2 (C), 138.0 (C), 129.1 (CH), 128.9 (CH), 128.6 (CH), 127.2 (CH), 124.3 (CH), 122.0 (C), 120.2 (CH), 117.8 (CH), 112.7 (CH), 112.6 (CH), 109.8 (CH), 70.9 (CH), 58.7 (CH), 54.5 (CH_3), 35.5 (CH_3); MS (relative intensity) 359 (M^+ + 1, 100), 358 (M^+, 29.0), 212 (24.2), 118 (23.7).

Anal. Calcd for $C_{23}H_{22}N_2O_2$: C, 77.09; H, 6.14; N, 7.82. Found: C, 77.17; H, 6.22; N, 7.80.

16b: mp 146–148 °C; IR 1740, 1590, 1495 cm^{-1}; ^1H NMR ($CDCl_3$) 7.5–6.7 (m, 14 H), 5.3 (d, 1 H, J = 2.5 Hz), 5.0 (d, 1 H, J = 2.5 Hz), 3.6 (s, 3 H), 3.0 (s, 3 H); ^{13}C NMR (APT) 165.3 (C), 156.9 (C), 148.9 (C), 137.3 (C), 129.3 (CH), 129.0 (CH), 128.9 (CH), 126.6 (CH), 124.5 (C), 124.1 (CH), 120.9 (CH), 118.6 (CH), 117.5 (CH), 114.6 (CH), 110.7 (CH), 76.3 (CH), 55.6 (CH), 55.2 (CH_3), 34.7 (CH_3); MS (relative intensity) 359 (M^+ + 1, 100) 358 (M^+, 30.4), 118 (24.2).

***cis*-1-Phenyl-3-(ethylphenylamino)-4-(*o*-methoxyphenyl)-2-azetidinone (17a) and *trans*-1-Phenyl-3-(ethylphenylamino)-4-(*o*-methoxyphenyl)-2-azetidinone (17b).** From 2.15 g of Ib and 2.1 g of the *N*-phenylimine of *o*-methoxybenzaldehyde, 1.7 g (46%) of **17a** and 0.3 g (8%) of **17b** were obtained.

17a: mp 105–107 °C; IR 1740, 1600, 1500 cm^{-1}; ^1H NMR ($CDCl_3$) 7.5–6.7 (m, 14 H), 5.67 (d, 1 H, J = 5.1), 5.54 (d, 1 H, J = 5.1), 3.5 (s, 3 H), 3.3 (m, 1 H), 2.8 (m, 1 H), 0.8 (t, 3 H); ^{13}C NMR (APT) 165.2 (C), 157.2 (C), 146.7 (C), 137.8 (C), 129.1 (CH), 129.0 (CH), 128.6 (CH), 127.2 (CH), 124.2 (CH), 122.6 (C), 120.2 (CH), 117.4 (CH), 117.3 (CH), 113.8 (CH), 109.9 (CH), 72.1 (CH), 58.9 (CH), 54.6 (CH_3), 43.1 (CH_2), 12.7 (CH_3); MS (relative intensity) 373 (M^+ + 1, 53.3), 372 (M^+, 81.2), 212 (46.1), 105 (100).

17b: mp 136–137 °C; IR 1740, 1595, 1500 cm^{-1}; ^1H NMR ($CDCl_3$) 7.5–6.6 (m, 14 H), 5.35 (d, 1 H, J = 2.1 Hz), 4.93 (d, 1 H, J = 2.1 Hz), 3.7 (s, 3 H), 3.6 (m, 2 H), 1.3 (t, 3 H); ^{13}C NMR 166.2, 157.8, 147.9, 138.1, 130.4, 130.1, 129.7, 127.4, 125.3, 124.7, 121.7, 119.1, 118.2, 115.7, 111.5, 76.2, 58.2, 56.0, 43.6, 14.6; MS (relative intensity) 373 (M^+ + 1, 100), 372 (M^+, 92.7), 212 (37.8).

***cis*-1-(*p*-Nitrophenyl)-3-(ethylphenylamino)-4-(*p*-methoxyphenyl)-2-azetidinone (18a) and *trans*-1-(*p*-Nitrophenyl)-3-(ethylphenylamino)-4-(*p*-methoxyphenyl)-2-azetidinone (18b).** From 2.15 g of Ib and 2.56 g of the *N*-(*p*-nitrophenyl)imine of *p*-methoxybenzaldehyde, 2.7 g (59%) of **18a** and 0.8 g (20%) of **18b** were obtained.

18a: mp 148–150 °C; IR 1745, 1590, 1490 cm^{-1}; ^1H NMR ($CDCl_3$) 8.2–6.7 (m, 13 H), 5.50 (d, 1 H, J = 5.1 Hz), 5.48 (d, 1 H, J = 5.1 Hz), 3.75 (s, 3 H), 3.8 (m, 1 H), 3.0 (m, 1 H), 1.0 (t, 3 H); ^{13}C NMR 164.8, 159.6, 146.4, 143.6, 142.7, 129.1, 128.2, 125.2, 124.6, 118.1, 117.3, 114.1, 113.1, 72.0, 62.8, 55.1, 43.9, 13.1; MS (relative intensity) 417 (M^+, 2.4), 256 (9.0), 240 (19.3), 131 (14.2), 105 (100.0).

18b: mp 205–207 °C; IR 1745, 1600, 1495 cm^{-1}; ^1H NMR ($CDCl_3$) 8.2–6.6 (m, 13 H), 4.95 (d, 1 H, J = 2.4 Hz), 4.88 (d, 1 H, J = 2.4 Hz), 3.8 (s, 3 H), 3.6 (m, 2 H), 1.2 (t, 3 H); ^{13}C NMR 165.7, 160.2, 146.9, 144.0, 142.3, 129.4, 127.6, 127.4, 125.2, 119.5, 117.4, 115.4, 115.0, 75.5, 63.3, 55.3, 43.9, 13.9; MS (relative intensity) 417 (M^+, 8.3), 239 (24.8), 132 (12.1), 105 (100.0).

***trans*-1-Phenyl-3-chloro-4-(*p*-chlorophenyl)-2-azetidinone (19).** A benzene solution of 0.9 g of chloroacetic acid was added through a septa to a benzene solution of 2.15 g of the *N*-phenylimine of *p*-chlorobenzaldehyde, 1.9 g of *p*-toluenesulfonyl chloride, and 4 g of triethylamine. The addition took 1 h and the solution was stirred at room temperature for an additional 2 h. The usual workup and column chromatography resulted in 0.8 g (28%) of pure crystalline **19**: mp 105–106 °C; IR 1765, 1610, 1490 cm^{-1}; ^1H NMR 7.5–7.3 (m, 9 H), 5.2 (d, 1 H, J = 2 Hz), 4.6 (d, 1 H, J = 2 Hz); ^{13}C NMR 160.4, 136.6, 135.5, 133.6, 129.7, 129.2, 127.5, 125.0, 117.5, 65.4, 63.1; MS (relative intensity) 293 (M^+ + 1, 15.5), 292 (M^+, 63.2), 214 (14.5), 174 (28.2), 137 (47.4).

***cis*-1-Phenyl-3-methoxy-4-phenyl-2-azetidinone (20).** This compound was prepared by the same procedure as described above in 52% yield: mp 139–141 °C; (lit.[4h] mp 141–142 °C); ^1H NMR ($CDCl_3$) 7.4–7.25 (m, 10 H), 5.2 (d, 1 H, J = 5 Hz), 4.8 (d, 1 H, J = 5 Hz), 3.1 (s, 3 H).

General Procedure for the Preparation of β-Lactams by the Acetic Anhydride–Sodium Acetate Method. A 1-g portion of (alkylarylamino)acetic acid hydrochloride was refluxed with 1 equiv of imine, 3 g of sodium acetate, and 10 mL of acetic anhydride. After 3 h, the mixture was poured into a cold 5% aqueous sodium hydroxide solution. The aqueous solution was extracted with methylene chloride and the extract was dried over magnesium sulfate. After evaporation of the solvent, the concentrated filtrate was subjected to column chromatography, which resulted in a pure crystalline product.

***cis*-1-(*p*-Methoxyphenyl)-3-(*p*-tolylmethylamino)-4-(*p*-nitrophenyl)-2-azetidinone (21).** From 1 g of Ic and 1.27 g of the *N*-(*p*-methoxyphenyl)imine of *p*-nitrobenzaldehyde, 0.5 g (26%) of crystalline product was obtained by column chromatography: mp 161–163 °C; ^1H NMR ($CDCl_3$) 7.8–6.8 (m, 12 H), 5.2 (d, 1 H, J = 4.6 Hz), 5.1 (d, 1 H, J = 4.6 Hz), 3.5 (s, 3 H), 2.4 (s, 3 H), 2.1 (s, 3 H); ^{13}C NMR (APT) 162.9 (C), 156.7 (C), 147.6 (C), 145.3 (C), 142.4 (C), 141.9 (C), 129.8 (CH), 128.0 (CH), 127.6 (C), 123.6 (CH), 118.4 (CH), 114.6 (CH), 112.4 (CH), 71.9 (CH), 62.1 (CH), 55.5 (CH_3), 35.8 (CH_3), 20.3 (CH_3).

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Registry No. 1, 120638-33-7; 2, 120638-34-8; 3, 120638-35-9; 4, 120638-36-0; 5, 120638-37-1; 6, 120638-38-2; 7, 120638-39-3; 8, 120638-40-6; 9, 120638-41-7; 10, 120638-42-8; 11, 120638-43-9; 12, 120638-44-0; 13, 120638-45-1; 14, 120638-46-2; 15, 120638-47-3; 16a, 120638-48-4; 16b, 120638-52-0; 17a, 120638-49-5; 17b, 120638-53-1; 18a, 120638-50-8; 18b, 120638-54-2; 19, 33949-30-3; 19a, 21911-75-1; 19b, 21911-78-4; 19c, 120547-25-3; 20, 33812-89-4; 21, 120638-51-9; PhCH=NPh, 538-51-2; PhCH=CHCH=NPh, 953-21-9; *p*-ClC_6H_4CH=NPh, 2362-79-0; PhCH=NBu-*t*, 6852-58-0; *p*-$MeOC_6H_4CH$=NC_6H_4OMe-*p*, 1749-08-2; PhCH=NC_6H_4OMe-*p*, 783-08-4; *o*-$NO_2C_6H_4CH$=NPh, 17064-77-6; *p*-$NO_2C_6H_4CH$=NC_6H_4OMe-*p*, 5455-87-8; *o*-$MeOC_6H_4CH$=NPh, 3369-37-7; *p*-$MeOC_6H_4CH$=$NC_6H_4NO_2$-*p*, 15450-66-5; $ClCH_2COOH$, 79-11-8; $MeOCH_2COOH$, 625-45-6.