New Synthesis of β-Lactams Based on Nitrone Cycloaddition to Nitroalkenes

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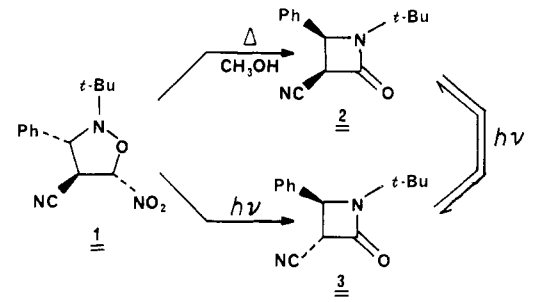
Heating a sample of the major 5-nitro-substituted isoxazolidine isomer obtained from the reaction of a *C*-phenyl-*N*-alkylnitrone with *trans*-1-cyano-2-nitroethylene in methanol resulted in ring contraction and formation of 4-phenyl-3-cyano-*N*-alkyl-2-azetidinone. The mechanism of this reaction involves removal of the acidic proton adjacent to the nitro group followed by N–O bond cleavage. The initially produced acyl nitro intermediate undergoes a subsequent cyclization under the reaction conditions. The photochemistry of the 5-nitro-substituted isoxazolidine was found to display a dependence on the wavelength of the exciting light. Pyrex-filtered light resulted in the elimination of nitrous acid whereas 2537-Å light produced the β-lactam system. The nature of the solvent and base used plays an important role in controlling the mode of reaction of the 5-nitro-substituted isoxazolidine. The essential requirements for ring contraction are proton activation toward base coupled with a facility for displacement by the neighboring nitrogen functionality.

Nitrones are members of a group of 1,3-dipolar compounds possessing octet stabilization but without an orthogonal double bond.[1,2] Cycloadditions of nitrones with monosubstituted olefins typically produce 5-substituted isoxazolidines with high regioselectivity.[3-8] It is well-known that, when two heteroatoms of higher electronegativity than carbon (e.g., nitrogen and oxygen) are linked together through a single bond, the bond-dissociation energy of such a linkage is considerably lower than that of a C–C single bond.[9,10] The origins of this effect are not at present clear, but repulsion between the necessarily higher nuclear charges and/or the nonbonded electron pairs may be responsible. Whatever its source, this effect represents a considerable driving force for the cleavage of the isoxazolidine ring. Thus, this heterocyclic system represents a substrate which can be readily reduced to provide access to γ-amino alcohols.[11-14] Reductive cleavage of the isoxazolidine ring has been extensively used in the synthesis of a wide range of natural products.[15] In a previous study we had reported that 5-nitro-substituted isoxazolidines represent convenient reagents for the synthesis of β-lactams.[16-23] New methods of constructing the four-membered lactam ring continue to be of interest in connection with the synthesis of analogues of the naturally occurring antibiotics.[24] In this paper we describe in detail a new procedure for the preparation of β-lactams. The key feature of the synthetic method involves 1,3-dipolar cycloaddition of a nitrone to a nitro-substituted olefin followed by a subsequent reorganization of the resulting 5-nitroisoxazolidine.

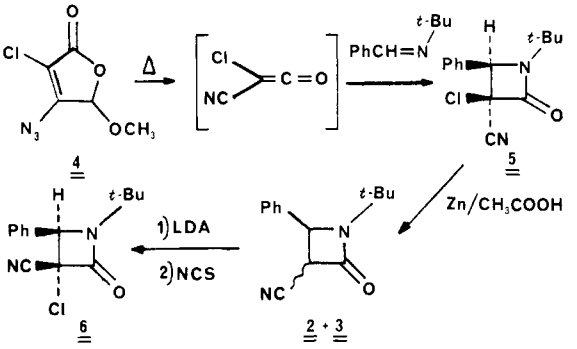
Results and Discussion

Heating a sample of 5-nitro-substituted isoxazolidine **1** in methanol gave cis β-lactam **2** (Scheme I) in quantitative yield: NMR ($CDCl_3$, 90 MHz) δ 1.15 (s, 9 H), 4.10 (d, 1 H, J = 6.0 Hz), 4.75 (d, 1 H, J = 6.0 Hz), 7.32 (s, 5 H). The thermal reorganization was found to be solvent dependent. Alcoholic solvents such as methanol or ethanol or polar aprotic solvents such as acetonitrile or acetone work best. No reaction occurred when benzene or hexane was used as the solvent. A similar reorganization occurred when isoxazolidine **1** was subjected to irradiation with 2537-Å light. In this case, however, the only product isolated was trans β-lactam **3**: NMR ($CDCl_3$, 90 MHz) δ 1.25 (s, 9 H), 3.65 (d, 1 H, J = 3.0 Hz), 5.80 (d, 1 H, J=3.0 Hz), 7.40 (s, 5 H). Extended photolysis of either the cis (**2**) or trans β-lactam (**3**) resulted in photoisomerization leading to a

Scheme I



Scheme II



(1) Huisgen, R.; Grashey, R.; Sauer, J. In "The Chemistry of Alkenes"; Patai, S., Ed.; Interscience: London, 1964; pp 806–878.
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(15) Tufariello, J. J. *Acc. Chem. Res.* **1979**, *12*, 396.
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† National Institutes of Health (Grant F32-GM08052) Postdoctoral Fellow.

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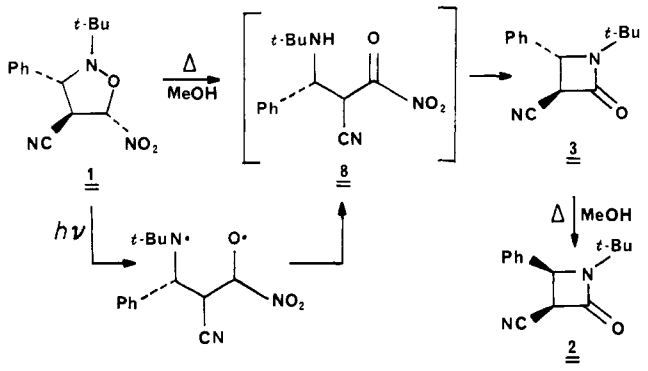
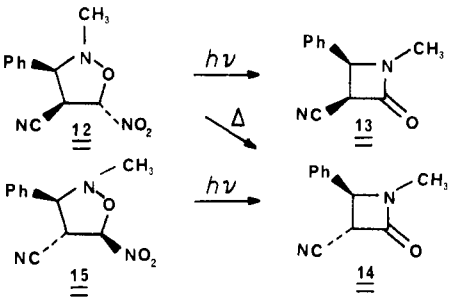
Scheme III



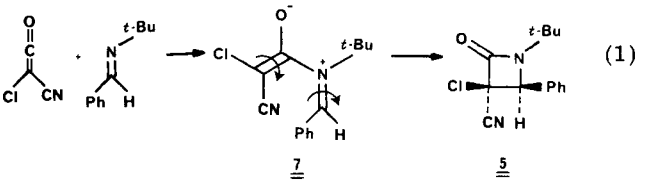
photostationary state ratio of 1:1. Trans β-lactam **3** was smoothly converted to the thermodynamically more stable cis isomer **2** on being heated in methanol with a trace of base. The stereochemistry of the cis and trans β-lactam rings can readily be assigned on the basis of the vicinal coupling constant (J_{cis} = 5.5–6.0 Hz vs. J_{trans} = 2.5–3.0 Hz).[25,26]

The structures of the β-lactams (i.e., **2** and **3**) were unambiguously established by comparison with independently synthesized samples. This was accomplished by heating 4-azido-3-chloro-5-methoxy-2(5*H*)-furanone (**4**) in the presence of *N*-benzylidene-*tert*-butylamine. Moore and co-workers have previously demonstrated that furanone **4** undergoes cleavage to chlorocyanoketene[27] which, in turn, is known to undergo [2 + 2] cycloaddition with C–N double bonds.[28,29] The major cycloadduct isolated from this reaction was assigned as (*Z*)-3-chloro-3-cyano-*N*-*tert*-butyl-4-phenyl-2-azetidinone (**5**, Scheme II). The stereochemistry is based primarily upon analogy to arguments previously developed by Moore and utilized in determination of the stereostructures of other members of this series.[30] An additional piece of evidence which was obtained in order to substantiate the stereochemistry of **5** involved treating β-lactam **2** (or **3**) with base followed by reaction with *N*-chlorosuccinimide. Under these conditions the corresponding (*E*)-chloroazetidinone **6** was obtained. The predominance of **6** was anticipated by reasonably assuming chlorination from the least hindered side of the enolate anion.[31] In addition, the ^{13}C NMR

Scheme IV



spectra of **5** and **6** reveal the cyano carbon in the latter to absorb at higher field (112 ppm) than in the former (114 ppm). This observation is in agreement with that previously reported for the *E* and *Z* isomers of a series of 3-chloro-3-cyano-2-azetidinones.[30] Treatment of either (*E*)-(**5**) or *Z*-chloroazetidinone (**6**) with zinc in acetic acid afforded a 9:2 mixture of cis (**2**) and trans (**3**) β-lactams. The exclusive formation of the (*Z*)-chloroazetidinone **5** from the [2 + 2] cycloaddition is probably a consequence of formation of the least sterically congested zwitterion represented by structure **7** (eq 1). Conrotatory electrocyclization of this species would be expected to give the *Z* stereoisomer.



(1)

The ready conversion of the 5-nitroisoxazolidine regioisomer (i.e., **1**) to the β-lactam ring is most easily rationalized by the mechanism outlined in Scheme III. The nitrogen–oxygen bond of **1** is expected to be cleaved readily, since such heteroatom–heteroatom bonds are known to be relatively weak.[9,32] Thus, removal of the acidic proton adjacent to the nitro group followed by N–O bond cleavage and subsequent cyclization of the transient acyl nitro intermediate **8** nicely accommodates the formation of the β-lactam system. Moreover, the rate of reorganization of the isoxazolidine ring to the β-lactam system is markedly enhanced in the presence of added base. The formation of cis lactam **2** from the thermolysis of **1** in methanol reflects thermodynamic rather than kinetic factors. We have demonstrated this by heating a pure sample of **3** in methanol and recovering only the cis isomer **2**. In this case, steric crowding about the β-lactam ring is minimized by having the cyano and phenyl groups trans to the very large *tert*-butyl group. This could account for the greater thermodynamic stability of the cis isomer.[33] Photolysis of isoxazolidine **1** results in N–O bond scission which is followed by internal hydrogen transfer and subsequent cyclization of intermediate **8**. It should be noted that the exclusive formation of lactam **3** from the irradiation of **1** fixes the stereochemistry of the phenyl and cyano groups as being trans in cycloadduct **1**. A related hydrogen atom transfer reaction of a *N*-alkylisoxazolidine has been reported by LeBel and provides good analogy for the

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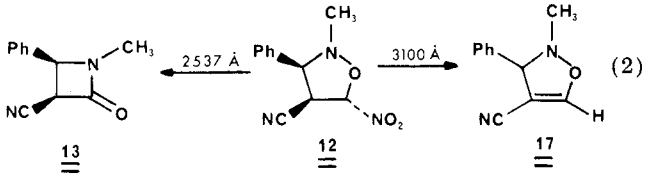
(30) Chambers, R.; Kunert, D.; Hernandez, L.; Mercer, F.; Moore, H. W. *Tetrahedron Lett.* **1978**, 933. Moore, H. W.; Hernandez, L.; Kunert, D. M.; Mercer, F.; Sing, A. *J. Am. Chem. Soc.* **1981**, *103*, 1769.
(31) Such stereospecificity in the halogenation of enolates of monocyclic 3-cyano-2-azetidinones has been unambiguously established (see ref 27).
(32) Baldwin, J. E.; Pudussery, R. G.; Qureshi, A. K.; Sklarz, B. B. *J. Am. Chem. Soc.* **1968**, *90*, 5326.
(33) A similar effect has been noted with the related arylaroylaziridine system. See: Lutz, R. E.; Turner, A. B. *J. Org. Chem.* **1968**, *33*, 516.

mechanism outlined in Scheme III.[34,35]

The chemical behavior of *N*-methyl-*trans*-4-cyano-5-nitro-*cis*-3-phenylisoxazolidine (**12**) was also studied. Irradiation of **12** in methanol at 2537 Å produced *N*-methyl-*cis*-3-cyano-4-phenyl-2-azetidinone (**13**) in 84% yield (Scheme IV). In marked contrast, heating a sample of **12** in acetonitrile produced the isomeric trans lactam **14**. Cis lactam **13** was converted into the thermdynamically more stable trans isomer **14** on refluxing in methanol. As was the case with the *tert*-butyl lactam system, azetidinones **13** and **14** were readily interconverted on extended photolysis (pss = 1:1). Irradiation of the trans 5-nitro-substituted isoxazolidine **15** was also investigated and was found to produce trans β-lactam **14** as the exclusive ring-contracted product. It should be noted that the distribution of β-lactams in the methyl series differs significantly from that encountered with the *tert*-butyl system. It is our belief that the difference in thermodynamic stability of the two lactam systems is chiefly controlled by the size of the substituent group on nitrogen. The structural assignment for β-lactams **13** and **14** was confirmed by comparison with independently synthesized samples prepared via the cyanoketene–imine cycloaddition route.[36]

The photochemistry of *N*-methylisoxazolidine **12** was found to display a remarkable dependence on the wavelength of the exciting light. Light of wavelength greater than 3100 Å resulted in the formation of 2,3-dihydroisoxazole **17** (92%), whereas 2537-Å light gave rise to β-lactam **13** (eq 2). The structure of **17** was unambiguously

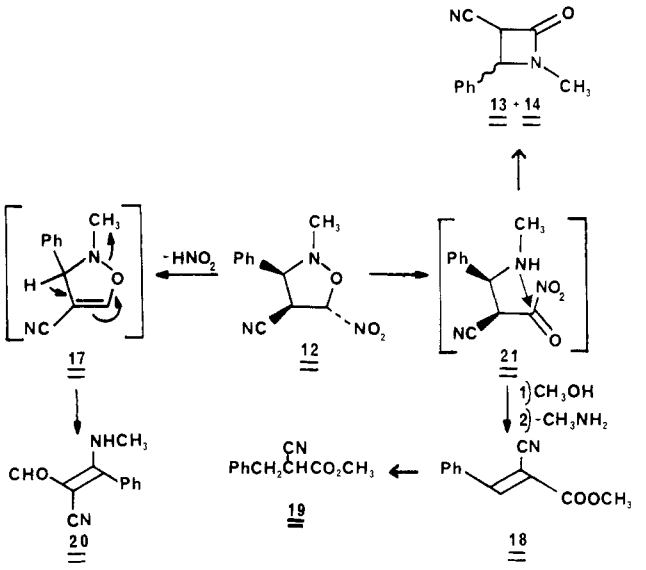


(2)

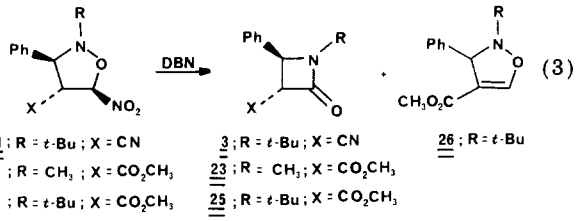
verified by comparison with an authentic sample prepared from the reaction of *C*-phenyl-*N*-methylnitrone with cyanoacetylene.[6] Each reaction must proceed with the virtual exclusion of the other since spectral monitoring of the reaction produced a nearly perfect isosbestic point. Irradiation of **12** with Pyrex-filtered light probably results in selective excitation of the n–π* state of the nitro chromophore.[37] This is followed by cleavage of the C–NO_2 bond and subsequent loss of a proton to give **17**. Related C–NO_2 bond fragmentations have been reported to occur with a variety of nitroaliphatic compounds.[37] Irradiation with 2537-Å light, on the other hand, proceeds by scission of the N–O bond of the isoxazolidine ring. The initially produced diradical will then undergo internal hydrogen transfer followed by cyclization to give the β-lactam system.

It is especially interesting to note that while the thermolysis of **12** in acetonitrile gave rise to the β-lactam ring, heating a sample of **12** in aqueous methanol resulted in the formation of three additional products. These were identified as methyl α-cyanocinnamate (**18**, 15%), methyl 2-cyano-3-phenylpropionate (**19**, 18%), and 3-amino-2-cyano-*N*-methyl-3-phenyl-2-propen-1-al (**20**, 27%). The structures of the compounds were assigned on the basis of their characteristic spectral data and by comparison with independently synthesized samples (see Experimental Section). In order to account for these products it becomes necessary to assume the intervention of several competing pathways. One route involves removal of the acidic proton adjacent to the nitro functionality followed by ring opening and internal cyclization to the lactam system. The initially produced acylnitro intermediate can also be attacked by methanol to give a transient amino ester. Elimination of methylamine from this species affords methyl α-cyanocinnamate (**18**, Scheme V). The formation of **19** is probably the result of a subsequent reduction of **18** under under the reaction conditions. The conversion of *N*-methylisoxazolidine **12** to propenal **20** proceeds by an entirely different pathway. Although information on the mechanistic details of this reaction is minimal, a tentative yet reasonable rationale can be advanced. Thus, elimination of nitrous acid from **12** will generate dihydroisoxazolidine **17** which can then undergo loss of a proton and concomitant N–O bond cleavage to give propenal **20**. The nature of the solvent system seems to play an important role in controlling the mode of reaction of *N*-methylisoxazolidine **12**. Elimination of nitrous acid is favored when highly polar solvents are used. This would suggest that the elimination reaction proceeds via a carbonium ion intermediate. This path is more likely to occur when solvents of high polarity are used.

Scheme V



In an effort to further establish the generality and scope of the nitrone-based synthesis of β-lactams, we studied the reaction of the 5-nitro-substituted isoxazolidine with various bases. Treatment of *N*-*tert*-butylisoxazolidine **1** with DBN in benzene resulted in a mixture of cis (**2**) and trans (**3**) β-lactams in quantitative yield (eq 3). A similar



(3)

1; R = *t*-Bu; X = CN
22; R = CH_3; X = CO_2CH_3
24; R = *t*-Bu; X = CO_2CH_3

3; R = *t*-Bu; X = CN
23; R = CH_3; X = CO_2CH_3
25; R = *t*-Bu; X = CO_2CH_3

26; R = *t*-Bu

result was obtained with the closely related 4-carbomethoxy-substituted system. Thus, treatment of **22** with DBN gave rise to trans β-lactam **23** in 90% yield. Reaction of the *N*-*tert*-butyl-substituted system (i.e., **24**) with DBN produced a mixture of β-lactam **25** (75%) as well as dihydroisoxazolidine **26** (20%).

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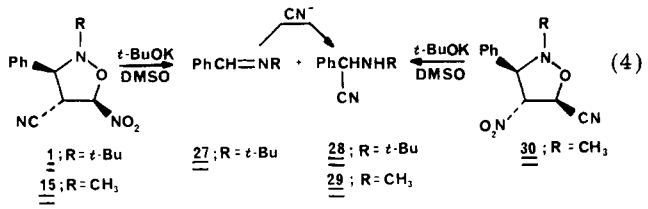
(35) Elderfield, R. C. "Heterocyclic Compounds"; Wiley: New York, 1957; Vol. 6, p 541.
(36) Bohme, H.; Ebel, S.; Hartke, K. *Chem. Ber.* **1965**, *98*, 1463.
(37) Morrison, H. A. "The Chemistry of the Nitro and Nitroso Groups"; Patai, S., Ed.; Wiley: New York, 1969, p 165.

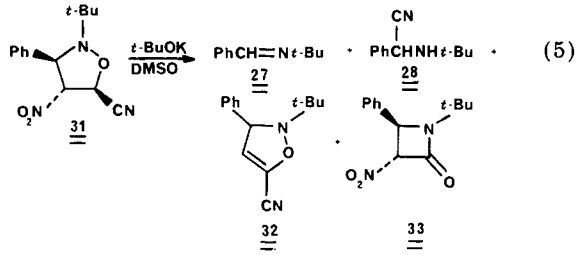
The base-induced behavior of the above systems was found to depend on the experimental conditions used. For example, treatment of isoxazolidine **1** with potassium *tert*-butoxide in dimethyl sulfoxide did not produce any detectable quantities of β-lactam **3**. Instead, the two products formed were identified as benzylidene-*tert*-butylamine (**27**) and α-cyano-*N*-*tert*-butylbenzylamine (**28**, eq 4). Reaction of *N*-methylisoxazolidine **15** with *tert*-



(4)

butoxide proceeded in an analogous fashion and afforded α-cyano-*N*-methylbenzylamine (**29**) as the exclusive product. This same compound was formed when the regioisomeric cycloadduct **30** was treated with *tert*-butoxide under conditions identical with those used for **15**. A mechanistic rationalization of the formation of **29** from the base treatment of either **15** or **30** is based on the premise that the initially generated carbanion induces N–O cleavage of the isoxazolidine ring. This step is followed by a subsequent elimination to generate imine **27** which then reacts with cyanide ion to give the final product. A control experiment established that imine **27** readily reacts with cyanide ion to give **28**.

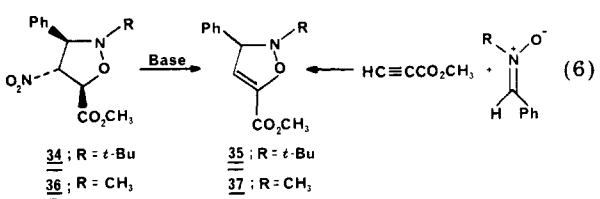
At this juncture it appeared worthwhile to determine whether the 5-cyano-substituted isoxazolidine would also undergo reorganization to the β-lactam system. To this end, we treated isoxazolidine **31** with potassium *tert*-butoxide in dimethyl sulfoxide (eq 5). In addition to com-



(5)

pounds **27** and **28**, two minor products (i.e., **32** (8%) and **33** (11%)) were also isolated. The fact that azetidinone **33** is formed demonstrates that the isoxazolidine to β-lactam transformation can be achieved with groups other than nitro in the 5-position of the heterocyclic ring. The essential requirements for the reaction are proton activation toward base coupled with a facility for displacement by the neighboring nitrogen functionality.

An entirely different mode of reaction was encountered when the substituent in the 5-position of the heterocyclic ring consists of a carbomethoxy group. Thus, treatment of *N*-*tert*-butyl-5-carbomethoxyisoxazolidine **34** with either DBN or potassium *tert*-butoxide resulted in the formation of dihydroisoxazole **35** (eq 6). The structure of this ma-



(6)

terial was verified by comparison with an independently synthesized sample prepared by treating *N*-*tert*-butylnitrone with methyl propiolate. An analogous result was obtained with the corresponding *N*-methyl derivative **36**.

In conclusion, we have shown that the major cycloadduct derived from the 1,3-dipolar cycloaddition of nitrones with a nitroethylene derivative undergoes a ready ring contraction to give the β-lactam ring. We are continuing to explore the scope and mechanistic features of the reaction and will report additional findings at a later date.

Experimental Section[38]

Photolysis of *trans*-4-Cyano-5-nitro-*trans*-3-phenyl-*N*-*tert*-butylisoxazolidine (1). A solution containing 200 mg of **1** in 150 mL of absolute methanol was photolyzed with a low-pressure mercury lamp (2537 Å) for 2.5 h. The solvent was removed under reduced pressure, leaving behind a pale oil which was fractionally recrystallized from an 8% acetone–hexane mixture to give *trans*-*N*-*tert*-butyl-3-cyano-4-phenyl-2-azetidinone (**3**): 57% yield; mp 180–181 °C; IR (KBr) 3000, 2980, 2300, 1750, 1560, 1460, 1380, 1240, 740 cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 7.40 (s, 5 H), 5.80 (*d*, *J* = 3.0 Hz, 1 H), 3.65 (d, *J* = 3.0 Hz, 1 H), 1.25 (s, 9 H); UV (95% ethanol) 210 nm (ε 11 000); MS, *m*/*e* 149, 146, 130, 129, 84, 58 (base). Anal. Calcd for $C_{14}H_{16}N_2O$: C, 73.65; H, 7.06; N, 12.27. Found: C, 73.63; H, 7.09; N, 12.25.

All attempts to further purify this material either by medium-pressure silica gel chromatography or by flash column chromatography led to the thermodynamically more stable cis β-lactam **2**: mp 91–92 °C (ethanol); IR (KBr) 3020, 2990, 1735, 1440, 1360, 1230, 700 cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 7.32 (s, 5 H), 4.75 (*d*, *J* = 6.0 Hz, 1 H), 4.10 (*d*, *J* = 6.0 Hz, 1 H), 1.15 (s, 9 H); ^{13}C NMR (20 MHz, $CDCl_3$) δ 157.97 (C=O), 135.09, 129.79, 129.37, 127.31 (aromatic), 113.25 (CN), 55.92 (C_2), 44.73 ($C(CH_3)_3$), 30.85 (C_3), 27.93 (CH_3); UV (95% ethanol) 210 nm (ε 2800); MS, *m*/*e* 149, 146, 130, 129, 82, 58 (base). Anal. Calcd for $C_{14}H_{16}N_2O$: C, 73.65; H, 7.06; N, 12.27. Found: C, 73.59; H, 7.07; N, 12.23.

The cis β-lactam **2** could also be prepared (90%) by gently heating (50 °C) a sample (300 mg) of isoxazolidine **1** in 5 mL of methanol for 15 min. The fact that the *cis*-*N*-*tert*-butyl-3-cyano-4-phenyl-2-azetidinone (**2**) is the thermodynamically more stable isomer was determined by heating a sample of the trans β-lactam **3** (20 mg) in 1 mL of deuterated acetone in a thick-walled NMR tube. The progress of the reaction was monitored by NMR spectroscopy. After 2 h, the trans β-lactam **3** has completely isomerized to the cis isomer. Furthermore, a solution containing the trans β-lactam (50 mg) in 20 mL of triethylamine was gently heated (40 °C) for 6 h. At the end of this period, all of the trans β-lactam had isomerized to the cis isomer.

Photostationary-State Interconversion of *cis*- and *trans*-*N*-*tert*-Butyl-3-cyano-4-phenyl-2-azetidinones (2 and 3). A solution containing 120 mg of cis β-lactam **2** in 40 mL of absolute methanol was irradiated in a quartz vessel with a low-pressure 2537-Å mercury arc lamp. The photolysis was periodically monitored for the disappearance of the cis β-lactam **2** by NMR spectroscopy. After 65 min, a 1:1 mixture of cis and trans β-lactams was present. This relative ratio remained constant even after 200 min of irradiation. The same photostationary state was achieved when the trans β-lactam **3** was subjected to similar photolysis conditions.

Independent Synthesis of *cis*- (2) and *trans*-*N*-*tert*-Butyl-3-cyano-4-phenyl-2-azetidinone (3). A solution containing 1.0 g of 3,4-dichloro-5-methoxy-2(5*H*)-furanone[27] in 7 mL of methanol was cooled to 0 °C by an ice bath. To this was added 0.382 g of sodium azide followed by stirring for 10 min in the ice bath. The ice bath was removed, and the reaction mixture was stirred for another 50 min. After the mixture has been stirred, 7 mL of water was added. The precipitate which formed after about 5 min was filtered and recrystallized from water–methanol to give 4-azido-3-chloro-5-methoxy-2(5*H*)-furanone: 0.85 g (82%);

(38) All melting points and boiling points are uncorrected. Elemental analyses were performed by Atlantic Microlabs, Atlanta, GA. The infrared absorption spectra were determined on a Perkin-Elmer 467 infrared spectrophotometer. The ultraviolet absorption spectra were measured with a Cary Model 14 recording spectrophotometer, using 1-cm matched cells. The proton magnetic resonance spectra were determined at 90 MHz by using a Varian EM-390 spectrometer. Mass spectra were determined with a Finnigan 4000 mass spectrometer at an ionizing voltage of 70 eV.

mp 66–67 °C; (lit.[27] mp 68–69 °C); NMR ($CDCl_3$, 90 MHz) δ 3.63 (s, 3 H), 5.13 (s, 1 H).

To a flame-dried, three-necked, 25-mL flask under nitrogen was added 0.41 g of dry *N*-benzylidene-*tert*-butylamine followed by 10 mL of dry benzene. The reaction mixture was heated to 60 °C. A solution of 0.47 g of the above azido-2(5*H*)-furanone in 5 mL of dry benzene was added over the course of 5 min as the reaction was heated to reflux. The reaction mixture was concentrated under reduced pressure and then filtered through a column of silica gel with methylene chloride to remove any polymer. The filtrate was concentrated in vacuo, and the solid product was recrystallized from heptane to give (*Z*)-3-chloro-3-cyano-*N*-*tert*-butyl-4-phenyl-2-azetidinone (**5**): 0.58 g (81%); mp 79–80 °C; IR (KBr) 3000, 2260, 1775, 1460, 1375, 1340, 1260, 1220, 1110, 770, 700 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.33 (s, 9 H), 5.21 (s, 1 H), 7.43 (s, 5 H); ^{13}C (20 MHz, $CDCl_3$) δ 27.93, 56.45, 59.23, 65.75, 114.42 (CN), 128.59, 128.72, 130.31, 132.57, 156.62; UV (95% ethanol) 205 nm (ε 11 900); MS, *m/e* 263 (M^+), 206, 165, 163, 128, 84, 77. Anal. Calcd for $C_{14}H_{15}N_2OCl$: C, 64.00; H, 5.75; N, 10.66. Found: C, 64.15; H, 5.78; N, 10.64.

A mixture of 116 mg of the above compound, 1 mL of glacial acetic acid, and 77 mg of powdered zinc in 15 mL of ether cooled to 0 °C was stirred for 2 h. The reaction mixture was allowed to warm to room temperature, filtered, and then washed with water and a 5% sodium bicarbonate solution. The organic phase was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The resulting oil was shown to be a 9:2 mixture of *cis*- (**2**) and *trans*-*N*-*tert*-butyl-3-cyano-4-phenyl-2-azetidinone (**3**). The spectral data of the isolated diastereomers were identical with those of the two β-lactams obtained from the photolysis of 4-cyano-5-nitro-3-phenyl-*N*-*tert*-butylisoxazolidine (**1**).

Preparation of (*E*)-3-Chloro-3-cyano-*N*-*tert*-butyl-4-phenyl-2-azetidinone (6). Into a flame-dried, 100-mL, round-bottomed flask were placed 60 mL of dry tetrahydrofuran and 155 mg of diisopropylamine. To the stirred solution was added dropwise with stirring 1.75 mL of a 1.5 M *n*-butyllithium solution. After the mixture was stirred for 30 min, a solution containing 600 mg of *cis*- (**2**) and *trans*-3-cyano-*N*-*tert*-butyl-4-phenyl-2-azetidinone (**3**) in 10 mL of dry tetrahydrofuran was added dropwise. The solution was allowed to stir at −75 °C for 1 h, and then 400 mg of *N*-chlorosuccinimide was added. After warming to room temperature, the solution was poured into water and extracted with ether. The ethereal solution was dried and concentrated under reduced pressure to give (*E*)-3-chloro-3-cyano-*N*-*tert*-butyl-4-phenyl-2-azetidinone (**6**) as a crystalline solid: 0.6 g (86%); mp 92–93 °C; IR (KBr) 3120, 2260, 1780, 1460, 1360, 1260, 1205, 1100, 765 cm^{-1}; UV (95% ethanol) 210 nm (ε 13 000); NMR ($CDCl_3$,90 MHz) δ 1.27 (s, 9 H), 4.82 (s, 1 H), 7.47 (s, 5 H); ^{13}C NMR (20 MHz, $CDCl_3$) δ 27.78, 56.48, 60.38, 69.29, 112.02 (CN), 127.29, 129.29, 130.62, 156.33; MS, *m/e* 263 (M^+), 229, 207, 165, 129. Anal. Calcd for $C_{14}H_{15}ClN_2O$: C, 64.00; H, 5.75; N, 10.66. Found: C, 64.18; H, 5.82; N, 10.60. Reduction of this material with zinc in acetic acid afforded a 9:2 mixture of cis (**2**) and trans (**3**) β-lactams.

Photolysis of *trans*-4-Cyano-5-nitro-*cis*-3-phenyl-*N*-methylisoxazolidine (12). The photolysis of **12** was found to be very wavelength dependent. When a solution containing 1.0 g of isoxazoline **12** in 400 mL of absolute methanol was photolyzed with a 550-W Hanovia lamp in a Pyrex well for 4 h, a clear oil was obtained after the removal of the solvent. This oil was subjected to medium-pressure silica gel column chromatography with a 10% acetone–hexane mixture as the eluent to give 920 mg of 4-cyano-2,3-dihydro-3-phenyl-*N*-methylisoxazole (**17**): 92% yield; mp 44–45 °C; IR (KBr) 3090, 2990, 2980, 2200, 1616, 1480, 1450, 1260, 1120 cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 7.25 (s, 5 H), 7.20 (d, *J* = 1.8 Hz, 1 H), 4.85 (d, *J* = 1.8 Hz, 1 H), 2.91 (d, 3 H). The spectral data obtained are identical with that reported for a pure sample of this compound.[6]

cis-Isoxazolidine **12** was also irradiated with 2537-Å light. A solution containing 500 mg of **12** in 120 mL of absolute methanol was degassed under an argon atmosphere and was then photolyzed for 1.5 h by using a 2537-Å low-pressure mercury lamp. The solvent was removed under reduced pressure, leaving behind a clear oil whose structure was assigned as *cis*-*N*-methyl-3-cyano-4-phenyl-2-azetidinone (**13**): 420 mg (84%); IR (KBr) 3010, 3000, 2300, 1740, 1500, 1460, 1380, 1250, 1110, 940, 820, 750 cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 7.62–7.30 (m, 5 H), 4.90 (d, *J* = 6.0 Hz, 1 H), 4.45 (d, *J* = 6.0 Hz, 1 H), 2.85 (d, 3 H). The cis β-lactam **13** rapidly isomerized to the more thermodynamically stable trans β-lactam **14** on purification. The structure of this material was verified by comparison with an authentic sample.[36]

A solution containing 30 mg of *trans*-isoxazolidine **15** in 60 mL of absolute methanol was irradiated for 1.5 h by using a 2537-Å low-pressure mercury lamp. After removal of the solvent, the resulting solid was recrystallized from methanol to give *trans*-*N*-methyl-3-cyano-4-phenyl-2-azetidinone (**14**): mp 87–88 °C (ethanol);[36] IR (KBr) 3020, 3000, 2920, 2120, 1770, 1490, 1450, 1420, 1250, 1000, 700 cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 7.60–7.25 (m, 5 H), 4.75 (d, *J* = 3.0 Hz, 1 H), 3.80 (d, *J* = 3.0 Hz, 1 H), 2.80 (s, 3 H); MS, *m/e* 186, 129 (base), 128, 118, 102, 77; ^{13}C (20 MHz, $CDCl_3$) 158.20 (C=O), 134.16, 130.08, 129.66, 126.78 (aromatic), 117.16 (CN), 60.42 (C_3), 47.36 (C_4), 27.96 (CH_3). Anal. Calcd for $C_{11}H_{10}N_2O$: C, 70.95; H, 5.41; N, 15.05. Found: C, 70.97; H, 5.43; N, 15.01.

Photostationary-State Interconversion of Cis and Trans β-Lactams 13 and 14. A solution containing 120 mg of pure trans β-lactam **14** in 60 mL of absolute methanol was irradiated in a quartz vessel with a low-pressure 2537-Å mercury arc lamp. The reaction was monitored by NMR spectroscopy for the disappearance of the trans β-lactam **14**. After 45 min of irradiation, the ratio of cis/trans β-lactams was 1.0/1.0. This ratio did not change even after 2 h of further irradiation. The same photostationary state was reached by using a pure sample of cis β-lactam **13**.

Attempted Preparation of 3-Chloro-3-cyano-*N*-methyl-4-phenylazetidinone. To a flamed-dried, three-necked, 50-mL, round-bottomed flask under nitrogen was added 0.62 g of *N*-benzylidenemethylamine followed by 20 mL of dry benzene. The solution was heated at 60 °C, and then a solution containing 1.0 g of 4-azido-3-chloro-5-methoxy-2(5*H*)-furanone in 10 mL of benzene was added over a 5-min period. The reaction mixture was heated at 60 °C for 20 h. The solution was concentrated under reduced pressure, and the residue was chromatographed on a silica gel chromatography column with benzene as the eluent. The major reaction product was identified as 5-chloro-5-cyano-1,3-dimethyl-2,6-diphenyl-1,2,5,6-tetrahydro-4(3*H*)-pyrimidinone (**16**) on the basis of its spectral properties: mp 166–167 °C; NMR ($CDCl_3$, 100 MHz) δ 2.15 (s, 3 H), 2.82 (s, 3 H), 4.47 (s, 1 H), 4.70 (s, 1 H), 7.07–7.57 (m, 10 H); ^{13}C NMR (20 MHz, $CDCl_3$) δ 32.64, 39.40, 57.22, 71.30, 79.79, 117.37, 128.38, 129.10, 129.32, 129.54, 129.90, 136.66, 158.97; IR (KBr) 3100, 2820, 2260, 1680, 1440, 1400, 1300, 1220, 1160, 850, 750, 695 cm^{-1}; UV (95% ethanol) 208 nm (ε 11 400); MS, *m/e* 304 (M^+), 262, 220, 185, 137, 118. Anal. Calcd for $C_{19}H_{18}N_3OCl$: C, 67.15; H, 5.34; N, 12.37. Found: C, 67.18; H, 5.24; N, 12.54.

Thermolysis of *trans*-4-Cyano-5-nitro-*cis*-3-phenyl-*N*-methylisoxazolidine (12) in Methanol. A 836-mg sample of **12** in 250 mL of absolute methanol was heated at 90 °C for 12 h. The solvent was removed under reduced pressure, and the clear oil obtained was subjected to silica gel flash column chromatography with a 10% acetone–hexane mixture as the eluent. The first material isolated was a white crystalline solid (15% yield; mp 86–87 °C) whose structure was assigned as methyl α-cyanocinnamate (**18**, lit.[39] mp 88–89 °C): IR (KBr) 3030, 3000, 2980, 1710, 1590, 1440, 1430, 900 cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 8.30 (s, 1 H), 8.15–7.90 (m, 2 H), 7.62–7.48 (m, 3 H). The spectral properties of this compound are identical with those of an authentic sample of methyl α-cyanocinnamate.[39] The second material isolated from the column (18% yield) was a clear oil which was further purified by molecular distillation (bp 110 °C (0.06 mm)) to give a white solid: mp 74–75 °C; IR (neat) 3080, 3000, 2300, 1750, 1620, 1520, 1460 cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 7.35 (s, 5 H), 3.90–3.60 (m, 4 H), 3.25–3.10 (m, 2 H); UV (95% ethanol) 305 nm (ε 2200); MS, *m/e* 189, 178, 156, 119, 105, 91, 77. Anal. Calcd for $C_{11}H_{11}NO_2$: C, 69.82; H, 5.86; N, 7.40. Found: C, 69.82; H, 5.86; N, 7.38.

On the basis of these properties, this material was assigned the structure of methyl 2-cyano-3-phenylpropionate (**19**). The

(39) Hayashi, T. *J. Org. Chem.* **1966**, *31*, 3253.

structure of this material was verified by comparison with independently synthesized material. A solution containing 1.0 g of methyl α-cyanocinnamate (18), 50 mg of 10% palladium on carbon, and 50 mL of ethyl acetate was subjected to hydrogenation for 6 h in a Paar shaker. Filtration of the catalyst followed by removal of the solvent under reduced pressure gave 950 mg of a white solid which was identical in every detail with the second component isolated from the chromatography column.

The third material eluted from the column corresponds to a 1:1 mixture of cis and trans β-lactams **13** and **14** in 14% yield. The last fraction obtained from the column was a white crystalline solid: mp 167–168 °C; 27% yield; IR (KBr) 3190, 3000, 2980, 2780, 2290, 1640, 1600, 1480, 1410, 1370, 810, 750 cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 9.40 (s, 1 H), 7.70–7.20 (m, 6 H), 2.90 (d, J = 6.0 Hz, 3 H); UV (95% ethanol) 310 nm (ε 11 000), 295 (8600); MS, m/e 187 (base), 186, 185, 158, 157, 130, 118, 77. Anal. Calcd for $C_{11}H_{10}N_2O$: C, 70.95; H, 5.41; N, 15.05. Found: C, 70.66; H, 5.46; N, 14.97.

On the basis of these properties this solid is assigned the structure of *N*-methyl-3-amino-3-phenyl-2-cyano-2-propen-1-al (**20**). Dihydroxazolidine **17** was also detected in ca. 3% yield in the crude reaction mixture.

Reaction of *trans*-*N*-*tert*-Butyl-5-cyano-4-nitro-3-phenylisoxazolidine with Potassium *tert*-Butoxide in Dimethyl Sulfoxide. A solution containing 500 mg of the 5-cyano-substituted isoxazolidine **31** in 10 mL of dry dimethyl sulfoxide was added dropwise to a solution containing 204 mg of potassium *tert*-butoxide in 5 mL of dimethyl sulfoxide. The resulting solution was allowed to stir to room temperature for 18 h. At the end of this time the solution was diluted with 100 mL of ether and washed with portions (5 × 100 mL) of water. The ether layer was dried over magnesium sulfate, and the solvent was removed under reduced pressure. The clear oily residue that was obtained was purified via flash column chromatography with an 8% acetone–hexane solution as the eluent. The first material eluted from the column was identifed as *N*-benzylidine-*tert*-butylamine (**27**, 42% yield). The second material eluted from the column was a clear oil (58% yield) whose structure was assigned as α-cyano-*N*-*tert*-butylbenzylamine (**28**) on the basis of its spectroscopic properties: IR (neat) 3450, 3090, 2900, 1490, 1440, 1360, 1230, 1090, 1020 cm^{-1}; NMR (90 MHz, CCl_4) δ 7.60–7.30 (m, 5 H), 4.65 (br s, 1 H), 1.3 (s, 9 H); UV (95% ethanol) 250 nm (ε 18 000); MS, m/e 154, 151, 116, 105, 91, 84, 77. Anal. Calcd for $C_{12}H_{16}N_2$: C, 76.55; H, 8.57; N, 14.88. Found: C, 75.49; H, 8.64; N, 14.69.

The structure of this material was further established by comparison with an independently synthesized sample. To a solution containing 1.0 g of *N*-*tert*-butyl-*N*-benzylideneamine, 50 mg of zinc chloride, and 20 mL of methylene chloride was added dropwise a solution containing 614 mg of trimethylsilyl cyanide in 10 mL of methylene chloride. After 1 h, the reaction mixture was treated with 10 mL of water and stirred for an additional h. Standard workup conditions gave 800 mg of **28** as a clear oil which was identical with the material obtained from the base treatment of **1**.

The third component isolated from the column was a crystalline solid: 8% yield; mp 106–107 °C; IR (KBr) 3100, 3010, 2990, 2200, 1620, 1480, 1440, 1370, 1350, 1220, 1190, 920 cm^{-1}; NMR (90 MHz, CCl_4) δ 7.4 (m, 5 H), 5.6 (d, J = 3.0 Hz, 1 H), 5.30 (d, J = 3.0 Hz, 1 H), 1.15 (s, 9 H); MS, m/e 172, 151, 127, 99, 85. Anal. Calcd for $C_{14}H_{16}N_2O$: C, 73.65; H, 7.06; N, 12.27. Found: C, 73.58; H, 7.09; N, 12.23.

On the basis of this data the structure of this material was assigned as 5-cyano-4,5-dehydro-*N*-*tert*-butyl-3-phenylisoxazolidine (**32**).

The last material eluted from the column was assigned as *trans*-*N*-*tert*-butyl-3-nitro-4-phenyl-2-azetidinone (**33**): mp 67–68 °C (pentane); 11% yield; IR (KBr) 3010, 3000, 1780, 1560, 1380, 1340, 1270, 1240, 760 cm^{-1}; NMR (90 MHz, CCl_4) δ 7.4 (s, 5 H), 5.18 (d, 1 H, J = 1.5 Hz), 5.02 (d, 1 H, J = 1.5 Hz), 1.30 (s, 9 H); MS, m/e 162, 150, 149, 105 (base), 91, 84, 77. Anal. Calcd for $C_{13}H_{16}N_2O_3$: C, 62.89; H, 6.50; N, 11.28. Found: C, 62.86; H, 6.53; N, 11.28.

Reaction of *trans*-*N*-*tert*-Butyl-3-phenyl-4-cyano-5-nitro-*trans*-3-phenylisoxazolidine (1) with Potassium *tert*-Butoxide in Dimethyl Sulfoxide. In a 100-mL round-bottomed flask were placed 481 mg of potassium *tert*-butoxide and 5 mL of dry dimethyl sulfoxide. To this was added 1.19 g of **1** in 10 mL of dimethyl sulfoxide. The resulting solution was stirred at 25 °C for 18 h and was then diluted with water and extracted with ether. The ether layer was dried over magnesium sulfate, and the solvent was removed under reduced pressure. The oily residue obtained was purified by flash silica gel chromatography with a 6% acetone–4% triethylamine–90% hexane mixture as the eluent. Two major products were obtained. The first component to be eluted was identified as *N*-benzylidine-*tert*-butylamine (**27**, 43% yield). The second fraction was a clear oil (57% yield) whose structure was established as α-cyano-*N*-*tert*-butylbenzylamine (**28**) by comparison with an authentic sample.

Reaction of *N*-*tert*-Butyl-3-phenyl-4-cyano-5-nitroisoxazolidine (1) with 1,5-Diazabicyclo[4.3.0]-5-nonene. A solution containing 226 mg of 1,5-diazabicyclo[4.3.0]-5-nonene in 40 mL of dry benzene was treated with 503 mg of **1** in 20 mL of benzene. The reaction mixture was stirred at 25 °C for 12 h and was then washed with water, with a 5% hydrochloric acid solution, and finally with a saturated sodium bicarbonate solution. The organic layer was dried over magnesium sulfate, and the solvent was removed under reduced pressure. The crystalline solid (464 mg) that was left behind was identified as a 1:1 mixture of *cis*- (**2**) and *trans*-*N*-*tert*-butyl-3-cyano-4-phenyl-2-azetidinone (**3**).

Reaction of *trans*-*N*-*tert*-Butyl-4-nitro-3-phenyl-*trans*-5-carbomethoxyisoxazolidine (34) with 1,5-Diazabicyclo[4.3.0]-5-nonene. A solution containing 145 mg of 1,5-diazabicyclo[4.3.0]-5-nonene in 20 mL of benzene was treated with 360 mg of **34** in 10 mL of benzene. The mixture was stirred at 25 °C for 12 h. The solvent was then removed at reduced pressure, and the solid residue that remained was recrystallized several times from hexane to give *N*-*tert*-butyl-3-phenyl-4,5-dehydro-5-carbomethoxyisoxazolidine (**35**): 72% yield; mp 82–83 °C; IR (KBr) 3000, 1730, 1655, 1500, 1480, 1460, 1390, 1375, 1355, 1320, 1260, 1205, 1120, 1080, 990, 770 cm^{-1}; NMR (90 MHz, CCl_4) δ 7.40–7.10 (m, 5 H), 5.60 (*d*, J = 3.0 Hz, 1 H), 5.22 (d, J = 3.0 Hz, 1 H), 3.75 (s, 3 H), 1.1 (s, 9 H); UV (95% ethanol) 282 nm (ε 2600); MS, m/e 261, 205, 184, 162, 128, 104, 77. Anal. Calcd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found: C, 68.87; H, 7.35; N, 5.32.

The structure of this material was verified by comparison with an independently synthesized sample. A solution containing 1.0 g of methyl propiolate and 2.10 g of *N*-*tert*-butylphenylnitrone in 150 mL of benzene was heated at reflux for 10 h. Removal of the solvent left an oily residue which was chromatographed on silica gel. The first component isolated from the column was a white solid (mp 82–83 °C) which was identical in every detail with a sample of **35** obtained from the base treatment of **34**. The second material isolated from the chromatography column was a clear oil whose structure was established as the isomeric 4-carbomethoxy-*N*-*tert*-butyl-3-phenyl-4,5-dehydroisoxazolidene: IR (neat) 3080, 3000, 1705, 1635, 1460, 1430, 1385, 1325, 1235, 1000, 935, 860 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.1 (s, 9 H), 3.50 (s, 3 H), 5.20 (d, 1 H, J = 1.5 Hz), 7.2–7.4 (m, 6 H); UV (95% ethanol) 272 nm (ε 5800); MS, m/e 261, 204, 184, 162, 128, 103, 77. Anal. Calcd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found: C, 68.70; H, 7.38; N, 5.33.

Reaction of *trans*-*N*-*tert*-Butyl-4-carbomethoxy-3-phenyl-*trans*-5-nitroisoxazolidine (24) with 1,5-Diazabicyclo[4.3.0]-5-nonene. A solution containing 80 mg of 1,5-diazabicyclo[4.3.0]-5-nonene and 10 mL of dry benzene was treated with 154 mg of **24** in 10 mL of benzene. The mixture was stirred at 25 °C for 18 h and was chromatographed through a small pad of silica gel. The major component obtained after removal of the solvent was a white crystalline solid [98 mg (75%); mp 119–120 °C (10% acetone–hexane)] whose structure was assigned as *trans*-*N*-*tert*-butyl-3-carbomethoxy-4-phenyl-2-azetidinone (**25**) on the basis of the spectroscopic data: IR (KBr) 3050, 3000, 1760, 1730, 1460, 1430, 1380, 1360, 1330, 1230, 1200, 1160 cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 7.40 (s, 5 H), 4.85 (d, J = 3.0 Hz, 1 H), 3.75 (s, 3 H), 3.70 (d, J = 3.0 Hz, 1 H), 1.25 (s, 9 H); MS, m/e 163, 162, 161, 131 (base), 103, 84, 77. Anal. Calcd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found: C, 68.88; H, 7.39; N, 5.34.

The second component isolated from the column was a clear oil (20%) whose structure was assigned as 4-carbomethoxy-*N*-*tert*-butyl-3-phenyl-4,5-dehydroisoxazolidine (**26**) by comparison

with an independently synthesized sample.

Reaction of *trans*-*N*-Methyl-4-carbomethoxy-3-phenyl-*trans*-5-nitroisoxazolidine (22) with 1,5-Diazabicyclo-[4.3.0]-5-nonene. In a 50-mL flask was added 576 mg of **22** in 20 mL of dry benzene. This solution was then treated with a solution containing 284 mg of DBN in 10 mL of benzene. After being stirred for 18 h at room temperature, the reaction mixture was filtered through a small pad of Florisil eluting with ether. The solvent was removed under reduced pressure to give an oil which was purified by preparative thin layer chromatography. The material obtained as a clear oil was identified as *trans*-*N*-methyl-3-carbomethoxy-4-phenyl-2-azetidinone (**23**): 69% yield; IR (neat) 3100, 2990, 2900, 1760, 1700, 1620, 1440, 1340, 1100 cm^{-1}; NMR (90 MHz, CCl_4) 7.3 (s, 5 H), 4.70 (d, 1 H, J = 3.0 Hz), 3.80 (br s, 4 H), 2.7 (s, 3 H); UV (95% ethanol) 270 nm (ϵ 1200); MS, m/e 219 (M^+), 191, 162, 161, 131 (base), 118, 105, 103, 77. Anal. Calcd for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.70; H, 6.07; N, 6.38.

Reaction of *trans*-*N*-Methyl-5-carbomethoxy-4-nitro-*trans*-3-phenylisoxazolidine (36) with Potassium *tert*-Butoxide in Dimethyl Sulfoxide. A solution containing 899 mg of **36** and 10 mL of dry dimethyl sulfoxide was treated with 503 mg of solid potassium *tert*-butoxide. After being stirred for 6 h at room temperature, the reaction mixture was diluted with ether and washed with water. The organic layer was dried over magnesium sulfate, and the solvent was removed under reduced pressure to give a clear oil which was purified by silica gel column chromatography with a 20% acetone–hexane mixture as the eluent. The major fraction corresponded to a colorless oil whose structure was assigned as *N*-methyl-5-carbomethoxy-3-phenyl-4,5-dehydroisoxazolidine (**37**): 70% yield; IR (neat) 3050, 3000, 2900, 1740, 1640, 1440, 1320, 1240 cm^{-1}; NMR (90 MHz, CCl_4) δ 7.30 (s, 5 H), 5.75 (*d*, J = 3.0 Hz, 1 H), 4.75 (d, J = 3.0 Hz, 1 H), 3.72 (s, 3 H), 2.8 (s, 3 H).

The structure of this material was further established by comparison with an independently synthesized sample. A mixture containing 100 mg of methyl propiolate and 230 mg of *N*-methylphenylnitrone in 25 mL of benzene was heated at reflux for 12 h. The solvent was removed under reduced pressure, and the residue was chromatographed on a silica gel column with a 20% ethyl acetate–hexane mixture as the eluent. The major component isolated (60%) was a clear oil whose structure was assigned as 4-carbomethoxy-*N*-methyl-3-phenyl-4,5-dehydroisoxazolidine on the basis of its spectral data: IR (neat) 3100, 3000, 2940, 1720, 1620, 1440, 1340, 1230, 1110, 740 cm^{-1}; NMR (CCl_4, 90 MHz) δ 2.80 (s, 3 H), 3.60 (s, 3 H), 4.75 (d, 1 H, J = 3.0 Hz), 7.1–7.4 (m, 6 H). The second material isolated from the column was identical in every detail with a sample of dihydroisoxazolidine **37** obtained from the base-induced reaction of **36**.

Reaction of *trans*-*N*-Methyl-4-cyano-5-nitro-3-phenylisoxazolidine (15) with 1,5-Diazabicyclo[4.3.0]-5-nonene. A solution containing 1.16 g of the 5-nitroisoxazolidine regioisomer **15** in 40 mL of dry benzene was treated with 0.67 g of DBN in 10 mL of benzene. After being stirred at 25 °C for 18 h, the reaction mixture was filtered through a silica gel column, and the filtrate was concentrated. The residue was purified by silica gel column chromatography to give a mixture of *cis*- and *trans*-*N*-methyl-3-cyano-4-phenyl-2-azetidinones (**13** and **14**, 50%) and *N*-methyl-α-cyanobenzylamine (**29**, 50%) as a clear oil which showed the following properties: IR (neat) 2950, 2250, 1660, 1440, 1240 cm^{-1}; NMR ($CDCl_3$, 60 MHz) δ 2.7 (s, 3 H), 4.70 (d, 1H, J = 4.0 Hz), 5.65 (d, 1 H, J = 4.0 Hz), 7.1 (s, 5 H).

Reaction of *trans*-*N*-Methyl-5-cyano-4-nitro-*trans*-3-phenylisoxazolidine (30) with 1,5-Diazabicyclo[4.3.0]-5-nonene. A solution containing 600 mg of **30** and 20 mL of dry benzene was treated with 260 mg of diazabicyclononene in 10 mL of dry benzene. The resulting solution was stirred at room temperature for 18 h after which the solution was filtered through a small pad of silica gel. The filtrate was concentrated under reduced pressure, and the residue was purified by flash column chromatography (10% acetone–hexane mixture). The major fraction contained 300 mg (79%) of *N*-methyl-α-cyanobenzylamine (**29**). The second minor component consisted of a clear oil whose structure was assigned as *N*-methyl-3-phenyl-5-cyano-4,5-dehydroisoxazolidine on the basis of its spectroscopic properties: IR (neat) 2950, 2250, 1660, 1440, 1240 cm^{-1}; NMR ($CDCl_3$, 60 MHz) δ 2.7 (s, 3 H), 4.70 (d, 1 H, J = 4.0 Hz), 5.65 (d, 1 H, J = 4.0 Hz), 7.1 (s, 5 H). Anal. Calcd for $C_{11}H_{10}N_2O$: C, 70.95; H, 5.41; N, 15.05. Found: C, 70.87; H, 5.39; N, 15.06.

Reaction of *N*-Methyl-3-phenyl-4-cyano-5-nitroisoxazolidine (15) with Potassium *tert*-Butoxide in Dimethyl Sulfoxide. To a mixture containing 1.91 g of potassium *tert*-butoxide in 20 mL of dry dimethyl sulfoxide was added 4.0 g of **15** in 10 mL of dimethyl sulfoxide. After being stirred for 12 h at 25 °C, the mixture was poured into 200 mL of water and extracted with ether. The ether layer was dried over magnesium sulfate, and the solvent was removed under reduced pressure. The resulting residue was subjected to molecular distillation (bp 48 °C (0.02 mm)) to give 500 mg of α-cyano-*N*-methylbenzylamine (**29**): IR (neat) 3350, 3050, 2950, 2800, 2250, 1640, 1480, 1440, 1360, 1100, 900 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.40–1.75 (br s, 1 H), 2.60 (s, 3 H), 4.80 (s, 1 H), 7.4–7.75 (m, 5 H); UV (95% ethanol) 245 nm (ϵ 18900); MS, m/e 119, 118 (base), 104, 102, 91, 77. Anal. Calcd for $C_9H_{10}N_2$: C, 73.94; H, 6.90; N, 19.16. Found: C, 73.87; H, 6.91; N, 19.13.

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