dissolved in DMF (0.2 mL) before being added to ammonia (75 mL) at −33 °C. Over 7 h, 5% Na–Hg amalgam (1 g) was added in five portions (200 mg each). After the reaction was complete, the solution was treated with solid NH_4Cl. The residue resulting from the evaporation of the ammonia was worked up by extraction. Flash chromatography provided acetonide **24b** (32 mg, 0.082 mmol, 65%) as a white foam: ^1H NMR ($CDCl_3$, δ ppm, 300 MHz) 7.84 (br s, 1 H), 7.54 (d, 1 H, J = 8.4 Hz), 7.6 (d, 1 H, J = 7.5 Hz), 7.15 (t, 1 H, J = 7.5 Hz), 7.08 (t, 1 H, J = 8.4 Hz), 4.18 (m, 2 H), 3.99 (dd, 1 H, J = 8.1, 2.1 Hz), 3.62 (s, 3 H), 3.25–3.09 (m, 3 H), 3.01 (dt, 1 H, J = 14.7, 3.3 Hz), 2.85–2.75 (m, 1 H), 2.68 (dd, 1 H, J = 10.8, 2.7 Hz), 2.64 (d, 1 H, J = 9.0 Hz), 2.18 (br s, 1 H), 2.68 (dd, 1 H, J = 10.8, 2.7 Hz), 2.64 (d, 1 H, J = 9.0 Hz), 2.18 (br s, 1 H), 2.17 (dd, 1 H, J = 14.7, 3.6 Hz), 1.75–1.65 (m, 2 H), 1.53 (s, 3 H), 1.35 (s, 3H); IR (KBr) 3387, 2927, 1725, 1208 cm^{-1}; CIMS (CH_4) m/z (rel intensity) 397 (M^+ + 1, 100), 396 (40).

20-Deethyl-15,20-*exo*,*exo*-dihydroxy-5,6-homocoronaridine (24c). The acetonide **24b** (44 mg, 0.11 mmol) was dissolved in MeOH (0.5 mL) followed by dropwise addition of concentrated HCl (1.0 mL). After 5 min, the solution was cooled to 0 °C and 20% aqueous Na_2CO_3 was added until basic. This solution was extracted with CH_2Cl_2, dried, and concentrated to yield **24c** (36 mg, 0.1 mmol, 92%) as a white foam: ^1H NMR ($CDCl_3$, δ ppm, 300 MHz) 7.95 (br s, 1 H), 7.53 (d, 1 H, J = 8.4 Hz), 7.29 (d, 1 H, J = 8.4 Hz), 7.17 (t, 1 H, J = 7.5 Hz), 7.11 (t, 1 H, J = 7.5 Hz), 4.41 (d, 1 H, J = 3.0 Hz), 3.81 (dd, 1 H, J = 7.5, 3.0 Hz), 3.74 (br d, 1 H, J = 7.5 Hz), 3.62 (s, 3 H), 3.31 (dt, 1 H, J = 10.5, 2.4 Hz), 3.28–3.2 (m, 1 H), 3.11 (q, 1 H, J = 7.5 Hz), 3.01 (dt, 1 H, J = 14.7, 2.7 Hz), 2.95 (dd, 1 H, J = 6.0, 3.0 Hz), 2.71 (qd, 1 H, J = 10.5, 3.0 Hz), 2.23 (br d, 1 H, J = 10.5 Hz), 2.1 (dd, 1 H, J = 14.7, 3.3 Hz), 2.01–1.9 (m, 2 H); IR (KBr) 3387, 3290, 2929, 1724, 1238 cm^{-1}; CIMS (CH_4) m/z (rel intensity) 357 (M^+ + 1, 100), 356 (20).

20-Deethyl-15,20-*exo*,*exo*-bis[(methylsulfonyl)oxy]-5,6-homocoronaridine (24e). The diol **24c** (35 mg, 0.1 mmol) was dissolved in CH_2Cl_2 (2 mL) followed by the addition of Et_3N (28 mg, 0.27 mmol, 2.8 equiv). After this mixture cooled to 0 °C, a catalytic amount of DMAP was added followed by methanesulfonyl chloride (28 mg, 0.24 mmol, 2.5 equiv). After 10 min at 0 °C, the solution was allowed to reach room temperature before being quenched with 20% aqueous Na_2CO_3. After workup, flash chromatography provided the dimesylate **24e** (26 mg, 0.05 mmol, 52%) as a white foam: ^1H NMR ($CDCl_3$, δ ppm, 300 MHz) 7.94 (br s, 1 H), 7.54 (d, 1 H, J = 7.5 Hz), 7.29 (d, 1 H, J = 7.5 Hz), 7.18 (t, 1 H, J = 7.5 Hz), 7.12 (t, 1 H, J = 7.5 Hz), 4.88 (dd, 1 H, J = 8.4, 3.9 Hz), 4.68 (d, 1 H, J = 8.4 Hz), 4.43 (br s, 1 H), 3.69 (s, 3 H), 3.3–3.19 (m, 3 H), 3.18 (s, 3 H), 3.13 (s, 3 H), 3.0 (dt, 1 H, J = 14.7, 4.5 Hz), 2.85–2.75 (m, 1 H), 2.68 (br d, 1 H, J = 13.5 Hz), 2.63 (br d, 1 H, J = 9.3 Hz), 2.44 (br s, 1 H), 2.37 (dd, 1 H, J = 14.7, 5.4 Hz), 1.89–1.75 (m, 2 H); IR (KBr) 3394, 2931, 1722, 1356, 1175 cm^{-1}; CIMS (CH_4) m/z (rel intensity) 513 (M^+ + 1, 100), 418 (20), 101 (60).

20-Deethyl-5,6-homocatharanthine (24f). The dimesylate **24e** (35 mg, 0.07 mmol) was dissolved in THF (8 mL) before being cooled to −42 °C. A stock solution of the naphthalene radical anion [prepared by stirring Na (23.4 mg, 1.02 mmol, 15 equiv) and naphthalene (131 mg, 1.02 mmol, 15 equiv) in THF (15 mL) at room temperature for 6 h] was cooled to −42 °C, and several aliquots were delivered (by canulla) to the THF solution of **24e**. The seventh aliquot caused the green color of the radical anion to persist. The solution was stirred for an additional 10 min, before being quenched with methanol. The reaction mixture was concentrated to a small volume and processed by the standard workup. Flash chromatography provided **24f** (14.3 mg, 0.05 mmol, 74%) as a white solid: ^1H NMR ($CDCl_3$, δ ppm, 300 MHz) 7.94 (br s, 1 H), 7.54 (d, 1 H, J = 7.5 Hz), 7.27 (d, 1 H, J = 7.5 Hz), 7.14 (t, 1 H, J = 7.5 Hz), 7.07 (t, 1 H, J = 7.5 Hz), 6.47 (t, 1 H, J = 6.3, 2.4 Hz), 6.44 (t, 1 H, J = 6.3 Hz), 4.96 (d, 1 H, J = 6.3 Hz), 3.57 (s, 3 H), 3.25 (q, 2 H, J = 5.5 Hz), 2.94 (qd, 1 H, J = 6.9, 3.0 Hz), 2.88–2.79 (m, 2 H), 2.72–2.64 (m, 2 H), 2.46 (dd, 1 H, J = 9.0, 2.4 Hz), 2.17–2.04 (m, 1 H), 1.98 (dd, 1 H, J = 12.6, 2.1 Hz), 1.95–1.81 (m, 1 H); IR ($CHCl_3$) 3332, 3008, 2827, 1713 cm^{-1}; ^{13}C NMR ($CDCl_3$) 173.8, 153.4, 134.4, 133.0, 128.7, 121.9, 119.2, 118.0, 110.9, 110.2, 55.3, 54.3, 52.9, 52.6, 52.2, 35.4, 31.0, 26.8, 21.5; CIMS (CH_4) m/z (rel intensity) 323 (M^+ + 1, 100), 322; HRMS exact mass calcd 322.1681, found 322.1665.

Acknowledgment. This research was supported by NIH Grant GM-41105. R.J.C. also received a DuPont Fellowship.

Supplementary Material Available: Brief description of the preparation and summary of the proton NMR peak positions are given for the following new compounds: **3d,e**, **4a–c**, **5**, **6e,f**, **7b,e,f**, **11b**, **12**, **13a–e**, **14a–c**, **18f–o**, **19c**, **23b–e**, **24d**; 300-MHz NMR spectra for compounds **16** and **17** (24 pages). Ordering information is given on any current masthead page.

Tandem Photochemical Synthesis of *N*-Amino β-Lactams from Pyrazolidin-3-ones

Steven T. Perri, Stacey C. Slater, Steven G. Toske, and James D. White*

Department of Chemistry, Oregon State University, Corvallis, Oregon 97331-4003

Received May 4, 1990

Substituted pyrazolidin-3-ones **8–13** were prepared by condensation of hydrazine hydrate with α,β-unsaturated carboxylic acids or esters and were converted to 1-(*o*-nitrobenzyl) derivatives **22–26**. Acylation of these heterocycles afforded 1-(*o*-nitrobenzyl)-2-acylpyrazolidin-3-ones **27–39** which, upon irradiation through Pyrex and then through Vycor, yielded 1-(acylamino)azetidin-2-ones **40–50**. Removal of the acyl residue from the extraannular nitrogen produced 1-aminoazetidin-2-ones **57–62**. Application of this route to *N*-amino β-lactams from pyrazolidin-3-one **67** resulted in **70** possessing the hydroxyethyl side chain characteristic of thienamycin. A mechanism is suggested for this tandem photochemical synthesis of β-lactams that involves initial removal of the N-1 *o*-nitrobenzyl substituent, followed by ring contraction via diazabicyclo[2.1.0]pentane intermediate **54**.

The presence of a β-lactam nucleus in the largest and most extensively used group of antibiotics has led to a broad effort directed toward synthesis of this ring system.[1] As the intense activity that had been focused on penicillins for over three decades began to wane in the 1970s, several new classes of β-lactam antibiotics emerged which were found to have valuable therapeutic properties.[2,3] These include the monocyclic β-lactams (monobactams),[4] a group

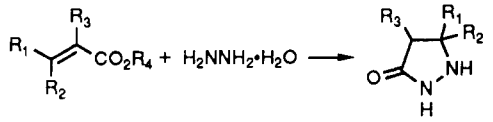
(1) Morin, R. B., Gorman, M., Eds. *Chemistry and Biology of β-Lactam Antibiotics*; Academic Press: New York, 1982; Vols. 1–3.

(2) Stapley, E. O. In *β-Lactam Antibiotics*; Salton, M., Shockman, G. D., Eds.; Academic Press: New York, 1981; p 327.

(3) Cooper, R. D. G. In *Topics in Antibiotic Chemistry*, Sammes, P. G., Ed.; Ellis Horwood; Chichester, 1979; Vol. 3, p 39.

0022-3263/90/1955-6037$02.50/0

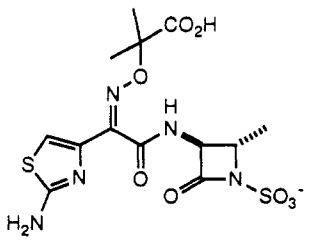
Table I. Synthesis of Pyrazolidin-3-ones from α,β-Unsaturated Acids and Esters



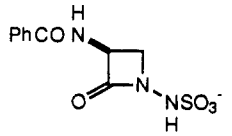
entry	R_1	R_2	R_3	R_4	method[a]	pyrazolidin-3-one (% yield)
1	H	H	CH_3	H	A	**8** (56)
2	CH_3	H	H	H	A	**9** (69)
3	CH_3	H	CH_3	H	A	**10** (83)
4	H	H	H	C_2H_5	B	**11** (24)
5	$CH_2CO_2C_2H_5$	H	H	C_2H_5	B	**12** (85)
6	Me	Me	H	C_2H_5	B	**13** (78)

[a] Method A: n-C_4H_9OH-C_6H_6, Al_2O_3 (cat.), reflux. Method B: C_2H_5OH, reflux.

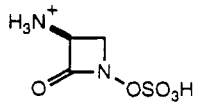
of "late generation" antibiotics that possess antibacterial activity comparable to penicillins and cephalosporins.[5] The first totally synthetic monobactam, aztreonam (1), exemplifies some of the attributes inherent in this family.[6]



1



2

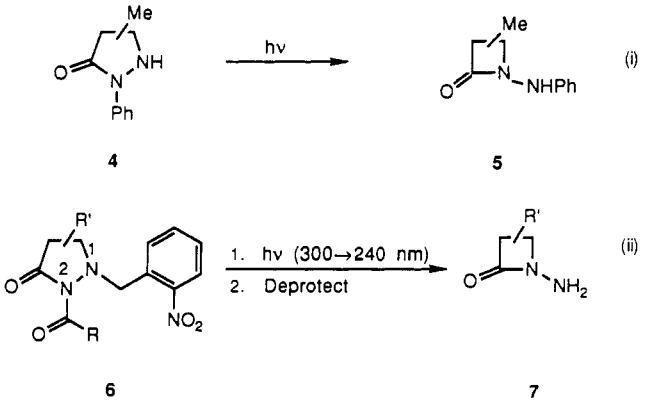


3

This resurgence of interest in β-lactams has prompted investigations into new and more versatile routes to their synthesis. Foremost among these is Miller's N-C_4 cyclization of hydroxamates to produce N-oxygenated azetidinones.[7] Our own efforts have concentrated on the synthesis of *N*-aminoazetidinones in the expectation that these systems will retain certain desirable properties of the monobactams, such as resistance to β-lactamase, while providing access to structural types, e.g. **2**, that are reported to have excellent antibacterial activity.[8] Substituted azetidinones such as **2** are nitrogen analogues of sulfactams, e.g. **3**,[9] which are known to be more stable than the parent monobactams. When substituted at C4, sulfactams are both inert to β-lactamase and orally active.[10]

Our goal from the outset was a photochemical synthesis of β-lactams using a ring contraction of easily prepared heterocyclic precursors. Although previous investigations of photochemical ring-contraction routes to β-lactams have met with only limited success,[11] a report by Ege that the pyrazolidin-3-one **4** affords *N*-aminoazetidinone **5** upon irradiation[12] (eq i) attracted our interest. This process was subsequently examined more fully by Johnson[13] and by Ege[14] but with somewhat disappointing results from the perspective of a practical route to β-lactam antibiotics.

With the dual objectives of defining the scope of the chemistry implicit in eq i and determining its prospect for the synthesis of monobactam antibiotics, we undertook a study of the photochemically induced ring contraction of certain pyrazolidin-3-ones. A key finding was that the overall efficiency of the β-lactam synthesis could be improved by a tandem photochemical sequence in which a photolabile protecting group (*o*-nitrobenzyl) was first introduced at N1. Photochemically induced ring contraction of the deblocked system followed (eq ii). The presence of an acyl substituent at N2 also contributes to successful ring contraction since photolysis of a pyrazolidin-3-one unsubstituted at N2 is reported to yield a β-lactam in very low (15%) yield.[13a] Herein we describe the preparation and photolysis of a series of 1-(*o*-nitrobenzyl)-2-acylpyrazolidin-3-ones **6** and conversion of the resultant azetidinones to novel *N*-amino β-lactams **7**.



4 5 (i)

6 7 (ii)

(4) (a) Imada, A.; Kitano, K.; Kintaka, K.; Muroi, M.; Asai, M. *Nature (London)* **1981**, *289*, 590. (b) Wells, J. S.; Trejo, W. H.; Principe, P. A.; Bush, K.; Georgopapadakou, N.; Bonner, D. P.; Sykes, R. P. *J. Antibiot.* **1982**, *35*, 295, 300. (c) Parker, W. L.; Koster, W. H.; Cimarusti, C. M.; Floyd, D. M.; Lui, W.-C.; Rathnum, M. L. *J. Antibiot.* **1982**, *35*, 189. (d) Sykes, R. B.; Cimarusti, C. M.; Bonner, D. P.; Bush, K.; Floyd, D. M.; Georgopapadakou, N. H.; Koster, W. H.; Liu, W. C.; Parker, W. L.; Principe, P. A.; Rathnum, M. L.; Slusarchyk, W. A.; Trejo, W. H.; Wells, J. S. *Nature (London)* **1981**, *291*, 489.

(5) (a) Cimarusti, C. M.: Sykes, R. B. *Med. Res. Rev.* **1984**, *4*, 1. (b) Bonner, D. P.; Sykes, R. B. *J. Antimicrob. Chemother.* **1984**, *14*, 313.

(6) Florey, K. *Analytical Profiles of Drug Substances*; Florey, K., Ed.; Academic Press: New York, 1988; Vol. 17, p 1.

(7) Miller, M. F. *Acc. Chem. Res.* **1986**, *19*, 49.

(8) Brewer, H.; Denzel, T. German Patent DE31 22 795A1.

(9) Gordon, E. M.; Ondetti, M. A.; Pluscec, J.; Cimarusti, C. M.; Bonner, D. P.; Sykes, R. B. *J. Am. Chem. Soc.* **1982**, *104*, 6053.

(10) Koster, W. H.; Slusarchyk, W. A.; Dejneka, T.; Kronenthal, D.; Perri, M. G.; Pilkiewicz, F. G.; Routh, F. L.; Sundeen, J. E.; Weaver, E. R.; Zahler, R. Twenty-fifth Interscience Conference on Antimicrobial Agents and Chemotherapy; Minneapolis, MN, 1985; Abstract 368.

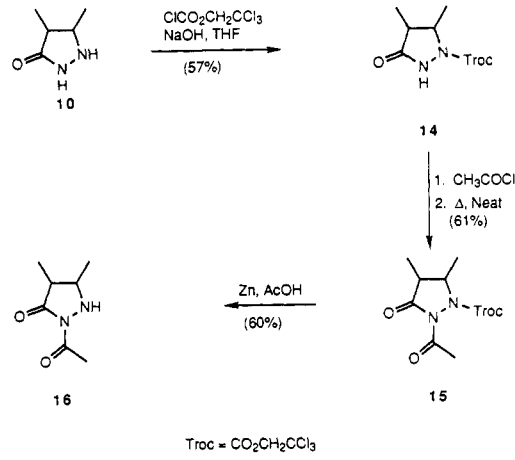
(11) (a) Lowe, G.; Ridley, D. *J. Chem. Soc., Perkin Trans. 1* **1973**, 2024. (b) Stork, G.; Szajewski, R. P. *J. Am. Chem. Soc.* **1974**, *96*, 5787. (c) Moore, H. W.; Hernandez, L., Jr.; Kuvert, D. M.; Mercer, F.; Sing, A. *J. Am. Chem. Soc.* **1981**, *103*, 1769. (d) St. Clair Black, D.; Boscacci, A. B. *J. Am. Chem. Soc. Chem Commun.* **1974**, 129. (e) Padwa, A.; Koehler, K. F.; Rodriguez, A. *J. Am. Chem. Soc.* **1981**, *103*, 4794. (f) Horokami, S.; Hirai, Y.; Nagata, M.; Yamazaki, T.; Date, T. *J. Org. Chem.* **1979**, *44*, 2083.

(12) (a) Ege, S. N. *J. Chem. Soc., Chem. Commun.* **1968**, 759. (b) Ege, S. N. *J. Chem. Soc. C* **1969**, 2624.

(13) (a) Johnson, P. Y.; Hatch, C. E. III *J. Org. Chem.* **1975**, *40*, 909. (b) Johnson, P. Y.; Hatch, C. E. III *J. Org. Chem.* **1975**, *40*, 3502.

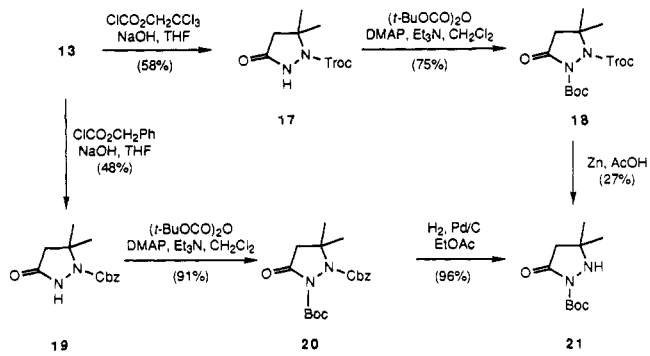
(14) Ege, S. N.; Butler, W. M.; Bergers, A.; Biesman, B. S.; Boerma, J. E.; Corondan, V. I.; Locke, K. D.; Meshinchi, S.; Ponas, S. H.; Spitzer, T. D. *J. Chem. Soc., Perkin Trans. 1*, **1983**, 1111.

Scheme I



Troc = $CO_2CH_2CCl_3$

Scheme II

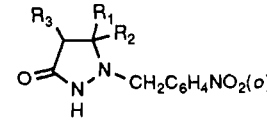


Results

Pyrazolidin-3-ones were prepared by condensation of hydrazine hydrate with either an α,β-unsaturated carboxylic acid[15] or with a corresponding ester,[16] as outlined in Table I. Reactions employing methacrylic, crotonic, and tiglic acids (entries 1–3) were carried out in a benzene–butanol mixture containing a small quantity of alumina, whereas α,β-unsaturated esters (entries 4–6) condensed smoothly with hydrazine hydrate in refluxing ethanol. Tiglic acid afforded a mixture of *cis*- and *trans*-4,5-dimethylpyrazolidin-3-ones (**10**), which were inseparable by chromatography. Subsequent transformations produced a pure derivative of cis **10** whose configuration was established by X-ray crystallographic analysis.

Previous studies of the photochemical contraction of pyrazolidinones to azetidinones imply that an anion stabilizing substituent is required at N2 of the pyrazolidinone for this conversion [13] and, since N1 is the more nucleophilic nitrogen atom in this heterocycle, it is necessary to block this site before acylation at N2 can be accomplished. Thus, **10** (mixture of cis and trans isomers) was treated with (2,2,2-trichloroethoxy)carbonyl (Troc) chloride to give **14** (Scheme I) which, upon acetylation, yielded **15**. Reductive removal of the Troc protecting group afforded cis and trans isomers of **16**, which could be separated by flash chromatography. However, attempts to extend this sequence to other pyrazolidinones encountered low yields. For example, although **13** could be protected as Troc derivative **17** and then acylated at N2 to give the Boc-substituted system **18**, reductive removal of the protecting group proceeded in low yield (Scheme II). The use of carbobenzyloxy (Cbz) protection of N1, as in **19**, mitigated this problem, since hydrogenolytic removal of the Cbz group from **20** afforded **21** in excellent yield.

Table II. Preparation of 1-(*o*-Nitrobenzyl)pyrazolidin-3-ones



starting materials	R_1	R_2	R_3	products	yield, %
8	H	H	CH_3	**22**	63
9	CH_3	H	H	**23**	56
10	CH_3	H	CH_3	**24**	71
11	H	H	H	**25**	65
12	$CH_2CO_2C_2H_5$	H	H	**26**	32

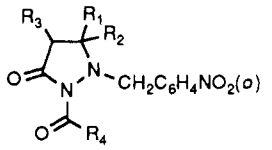
In practice, however, the most attractive solution to the problem of introducing an acyl group at N2 of these pyrazolidinones was found to be through the use of a photoremovable protecting group at N1. It was recognized that a judicious choice of the photolabile blocking group would enable the photochemical ring contraction to be carried out in tandem with cleavage at N1. Two requirements for successful implementation of this tandem photochemical process were (a) the photoreactive protecting group must be removed from N1 before reaction of the pyrazolidinone nucleus ensues, and (b) photoproducts generated in the N1 deprotection step should not interfere with subsequent azetidinone formation. The *o*-nitrobenzyl substituent[17] was found to meet these requirements and a series of 1-(*o*-nitrobenzyl)pyrazolidin-3-ones was prepared as shown in Table II. Alkylation of pyrazolidinones **8–12** with *o*-nitrobenzyl chloride in DMF in the presence of sodium iodide and triethylamine yielded the 1-substituted derivatives **22–26**.

The critical selection of an acyl substituent for N2 of pyrazolidinones **22–26** was based in part on its stability toward light and in part on the projected ease of removal after ring contraction. Since the properties of *N*-aminoazetidinones are largely unknown, the inertness of the four-membered ring toward conditions that would remove functionality from the extraanular nitrogen could not be confidently predicted. For this reason a variety of acyl substituents that included both acetyl and ester residues were substituted at N2 of the (*o*-nitrobenzyl)-pyrazolidinones. These are summarized in Table III.

Acetyl derivatives **27** and **33** were obtained by a standard procedure, and benzyl (Cbz) and ethyl carbamates **29** and **32** were prepared from the corresponding chloroformate esters. For Boc derivatives **28**, **34**, **35**, and **38** it was found most convenient to employ *tert*-butoxycarbonic anhydride in the presence of 4-(dimethylamino)pyridine.[18] The [2-(trimethylsilyl)ethoxy]carbonyl derivatives **30**, **31**, **36**, **37**, and **39** were prepared by the method of Carpino[19] using 2-(trimethylsilyl)ethyl azidoformate. Many of the urethanes prepared according to the procedures shown in Table III exhibited syn/anti isomerism about the N2–CO bond, but, in general, these compounds were easily purified by chromatography or crystallization. In particular, the cis and trans isomers of **36** were separated by flash chromatography and the configuration of the crystalline *cis*-4,5-dimethylpyrazolidin-3-one was established by an X-ray

(15) Rabini, T.; Vita, G. *J. Org. Chem.* **1965**, *30*, 2486.
(16) Stetter, H.; Findeinsen, K. *Chem. Ber.* **1965**, *98*, 3228.
(17) Amit, B.; Zehavi, U.; Patchornik, A. *J. Org. Chem.* **1974**, *39*, 192.
(18) Carpino, L. A. *Acc. Chem. Res.* **1973**, *6*, 191.
(19) Carpino, L. A.; Tsao, J.-H.; Ringsdorf, H.; Fell, E.; Hettrich, G. *J. Chem. Soc., Chem. Commun.* **1978**, 358.

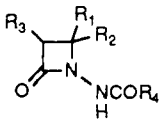
Table III. Preparation of 1-(*o*-Nitrobenzyl)-2-acylpyrazolidin-3-ones



starting materials	R_1	R_2	R_3	R_4	products	conditions[a]	yield, %
22	H	H	CH_3	CH_3	**27**	C	77
22	H	H	CH_3	O-*t*-C_4H_9	**28**	B	98
22	H	H	CH_3	$OCH_2C_6H_5$	**29**	A	73
22	H	H	CH_3	$OCH_2CH_2SiMe_3$	**30**	D	73
23	CH_3	H	H	$OCH_2CH_2SiMe_3$	**31**	D	81
23	CH_3	H	H	OCH_2CH_3	**32**	E	73
23	CH_3	H	H	CH_3	**33**	C	82
23	CH_3	H	H	O-*t*-C_4H_9	**34**	B	96
24	CH_3	H	CH_3	O-*t*-C_4H_9	**35**	B	99
24	CH_3	H	CH_3	$OCH_2CH_2SiMe_3$	**36**	D	59[b]
25	H	H	H	$OCH_2CH_2SiMe_3$	**37**	D	90
26	$CH_2CO_2C_2H_5$	H	H	O-*t*-C_4H_9	**38**	B	94
26	$CH_2CO_2C_2H_5$	H	H	$OCH_2CH_2SiMe_3$	**39**	D	90

[a] Conditions: (A) (i) $ClCO_2CH_2C_6H_5$, Et_3N, THF; (ii) 110 °C, neat, 9 h; (B) $(t\text{-}C_4H_9OCO)_2O$, DMAP, Et_3N, CH_2Cl_2; (C) (i) CH_3COCl, Et_3N, THF; (ii) 110 °C, neat; (D) $N_3CO_2CH_2CH_2SiMe_3$, NaH, THF, 0 → 25 °C; (E) (i) $ClCO_2C_2H_5$, Et_3N, THF; (ii) 110 °C, neat, 8 h. [b] 32% cis isomer, 27% trans isomer after chromatographic separation.

Table IV. Tandem Photochemical Conversion of Pyrazolidin-3-ones to 1-(Acylamino)azetidin-2-ones



starting materials	R_1	R_2	R_3	R_4	products	yield, %
28	H	H	CH_3	O-*t*-C_4H_9	**40**	84
29	H	H	CH_3	$OCH_2C_6H_5$	**41**	17
30	H	H	CH_3	$OCH_2CH_2SiMe_3$	**42**	60
31	CH_3	H	H	$OCH_2CH_2SiMe_3$	**43**	44
34	CH_3	H	H	O-*t*-C_4H_9	**44**	65
35	CH_3	H	CH_3	O-*t*-C_4H_9	**45**	79
36 (cis)	CH_3	H	CH_3	$OCH_2CH_2SiMe_3$	**46** (cis)	55
36 (trans)	CH_3	H	CH_3	$OCH_2CH_2SiMe_3$	**47** (trans)	51
37	H	H	H	$OCH_2CH_2SiMe_3$	**48**	34
38	$CH_2CO_2C_2H_5$	H	H	O-*t*-C_4H_9	**49**	58
39	$CH_2CO_2C_2H_5$	H	H	$OCH_2CH_2SiMe_3$	**50**	41

structure determination (Figure 1).

Irradiation of pyrazolidinones **28–31** and **34–39** were carried out in ethanol with a 450-W medium-pressure Hanovia lamp. After photolysis of the solution through a Pyrex filter for 1 h the filter was replaced by Vycor glass, and the mixture was irradiated for further 2 h. Azetidinones **40–50** were isolated in pure form by flash chromatography and were characterized by the presence of carbonyl absorption in their IR spectra at 1735 and 1780 cm^{-1}. The results are summarized in Table IV.

A plausible pathway for the sequence of steps that leads from a 1-(*o*-nitrobenzyl)-2-acylpyrazolidin-3-one **51** to a *N*-(acylamino)azetidin-2-one **55** is shown in Scheme III. The initial event, excitation and cleavage of the *o*-nitrobenzyl group, occurs readily at >300 nm,[17] giving *o*-nitrosobenzaldehyde (**52**)[20] and the N1-unsubstituted pyrazolidinone **53**. The latter is unreactive to light through Pyrex and, if the photolysis is interrupted at this stage, it can be isolated. However, at shorter wavelengths (<300 nm), **53** undergoes ring contraction through a presumed bicyclic intermediate **54**.[21] A 2-acyl substituent assists the ring contraction process by facilitating cleavage of the external C–N bond of the diaziridine ring in **54**, thus ensuring that **54** does not return to **53**. Related to this hypothetical pathway is the observation that β-lactam **56**, obtained upon photolysis of **21** through Vycor, reverted

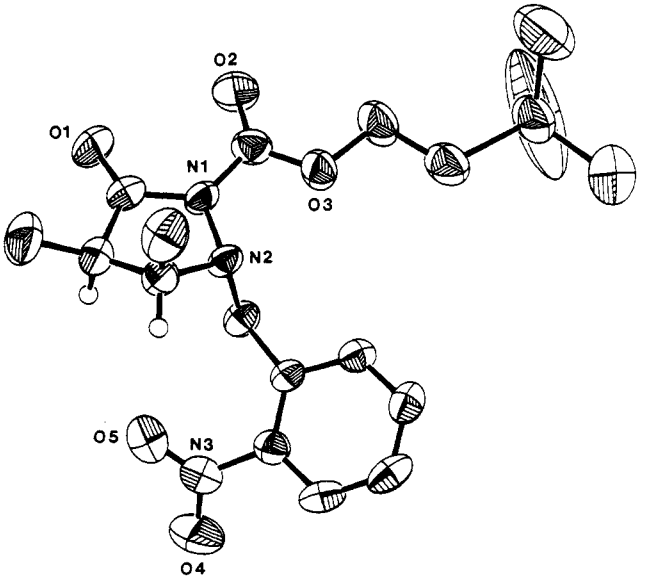
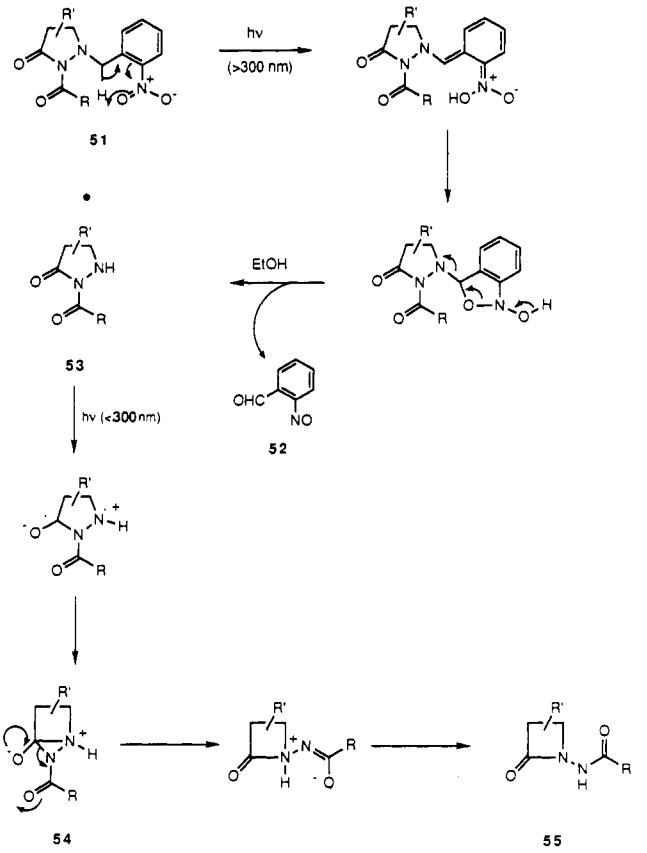


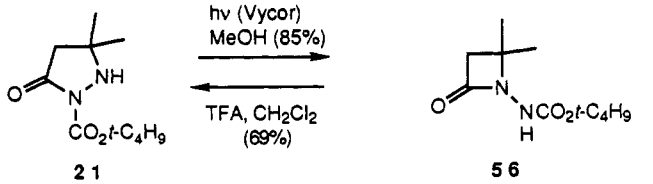
Figure 1. ORTEP drawing of *cis*-**36** with heteroatoms labeled. Thermal ellipsoids are drawn at the 50% probability level.

(20) Kalbag, S. M.; Roeske, R. W. *J. Am. Chem. Soc.* **1975**, *97*, 440.
(21) Cf.: Beak, P.; Messer, W. R. In *Organic Photochemistry*; Chapman, O. L., Ed.; Marcel Dekker: New York, 1969; Vol. 2, p 139.

Scheme III



to the pyrazolidinone upon exposure to trifluoroacetic acid. This result, which is analogous to an earlier observation by Testa,[22] may also be explained by the intervention of a diazabicyclo[2.1.0]pentane intermediate.

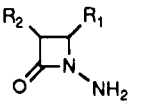


The apparent sensitivity of the *N*-aminoazetidinone system toward acidic reagents made clean removal of the Boc group from **40**, **44**, **45**, **49**, and **56** impossible. Although hydrogenolysis of the Cbz group in **41** produced the aminoazetidinone **57** in high yield, the inefficient preparation of **41** nullified this strategy. In contrast, a practical route to *N*-aminoazetidinones was found through cleavage of the [2-(trimethylsilyl)ethoxy]carbonyl derivatives,[23] and treatment of **42** and **43** and **46**–**48** with tetra-*n*-butylammonium fluoride gave **57**–**61** in good yield. The low yield obtained with **50** appears to be due to the instability of **62**.

Extension of this photochemical azetidinone synthesis to a system bearing the hydroxyethyl side chain characteristic of thienamycin (**63**) was suggested by a recent report from the Lilly Laboratories in which the preparation of pyrazolidinone **65** was described.[24] The latter was obtained as a 1:1 mixture with its diastereoisomer from

(22) Pifferi, G.; Consonni, P.; Testa, E. *Gazz. Chim. Ital.* **1967**, *97*, 1719.
(23) Carpino, L. A.; San, A. C. *J. Chem. Soc., Chem. Commun.* **1979**, 514.
(24) Jungheim, L. N. *Tetrahedron Lett.* **1989**, *30*, 1889.

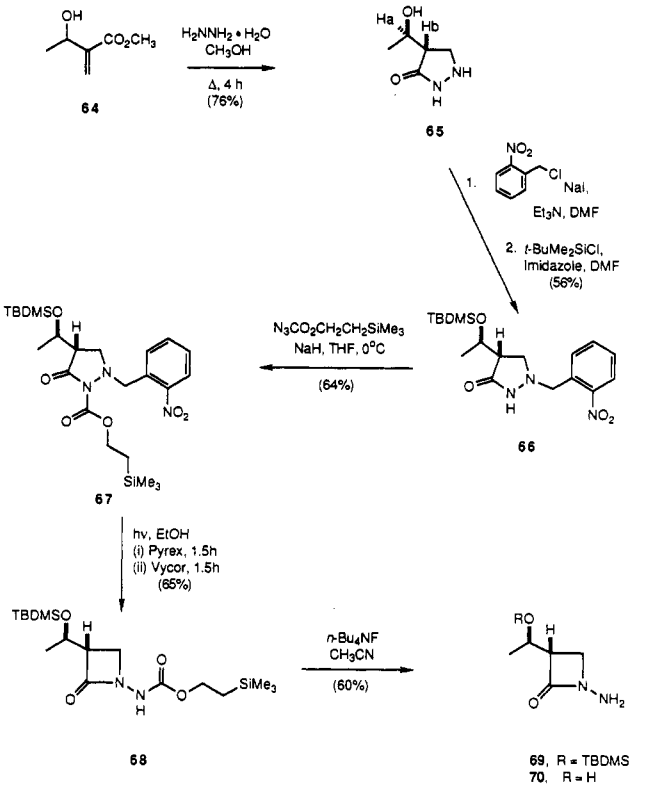
Table V. Preparation of 1-Aminoazetidin-2-ones



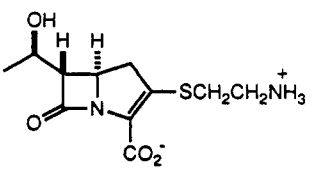
starting materials	R_1	R_2	products	conditions[a]	yield, %
41	H	CH_3	**57**	A	75
42	H	CH_3	**57**	B	73
43	CH_3	H	**58**	B	58
46 (cis)	CH_3	CH_3	**59** (cis)	B	73
47 (trans)	CH_3	CH_3	**60** (trans)	B	84
48	H	H	**61**	B	88
50	$CH_2CO_2C_2H_5$	H	**62**	B	33

[a] Conditions: (A) H_2, Pd/C, EtOAc; (B) $(n\text{-}C_4H_9)_4NF$, CH_3CN, 50 °C.

Scheme IV



the reaction of hydrazine hydrate with hydroxy ester **64**[25] and was separated chromatographically (Scheme IV). Stereochemical assignment to **65** was made on the basis of the H_a–H_b coupling constant (J = 2 Hz).[24]



63

Treatment of **65** with *o*-nitrobenzyl chloride afforded the expected 1-alkylated pyrazolidinone which, without purification, was converted to its *tert*-butyldimethylsilyl (TBDMS) ether **66**. Acylation at N2 of **66** was accomplished with 2-(trimethylsilyl)ethyl azidoformate,[19] and the

(25) Hoffmann, H. M. R.; Rabe, J. *J. Org. Chem.* **1985**, *50*, 3849.

resulting pyrazolidinone **67** was photolyzed, first through Pyrex and then through Vycor, to yield azetidinone **68**. It proved possible to selectively unmask the amino function of **68** by brief contact with tetra-*n*-butylammonium fluoride in acetonitrile, affording **69**. Upon prolonged (24 h) exposure to this reagent, **68** yielded the amino alcohol **70**.

In summary, the tandem photochemical route to *N*-amino β-lactams described above has potentially broad utility for the synthesis not only of aza analogues of sulfactams but of other monobactam derivatives as well. A pivotal advance in this area will be replacement of the amino group at the lactam nitrogen by other functionality (e.g. OH) and, along these lines, we are currently investigating the tandem photochemistry of 2-(*o*-nitrobenzyl)-isoxazolidin-5-ones.

Experimental Section

Solvents and Reagents. Commercial grade reagents were used without further purification except as indicated below. Hexane, ethyl acetate, acetyl chloride, and dimethylformamide were distilled prior to use. Methylene chloride was distilled from calcium hydride. Tetrahydrofuran and ether were distilled from potassium benzophenone ketyl. Column chromatography was performed using silica gel (230–400 mesh). Air-sensitive reactions were carried out in flame-dried glassware under a positive stream of argon. Reaction solutions were concentrated using a rotary evaporator at 30–50 mmHg.

General Procedure for the Preparation of Pyrazolidin-3-ones by Condensation of α,β-Unsaturated Carboxylic Acids with Hydrazine Hydrate. As a typical example, the condensation of methacrylic acid with hydrazine hydrate was carried out in the following manner. **4-Methylpyrazolidin-3-one (8).** To a solution of methacrylic acid (10.00 g, 0.116 mmol) in 12 mL of butanol was added hydrazine hydrate (7.76 mL, 0.16 mmol) and neutral alumina (80–200 mesh) in a 50-mL 3-necked flask equiped with a thermometer, a Dean-Stark trap, and an addition funnel. The suspension was heated and stirred at a bath temperature of 130 °C while the internal temperature was maintained at 94–95 °C by the addition of benzene from a funnel. The suspension was heated at reflux with a 94–95 °C internal temperature while water was withdrawn from the reaction. The reaction was continued for 8 h and then filtered hot through a bed of Celite and rinsed with hot butanol. The resulting solution was then concentrated in vacuo to a viscous oil. Vacuum distillation of the crude product was not carried out since the material polymerized readily upon heating. Purification by column chromatography on silica gel with 6% methanol–chloroform as the elutant yielded 6.45 g (56%) of **8**[16] as a viscous oil: IR (neat) 3200, 1681, 927 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.18 (d, J = 9.0 Hz, 3 H), 2.63 (m, 1 H), 3.04 (t, J = 14.2 Hz, 1 H), 3.64 (dd, J = 9.0, 14.2 Hz, 1 H); MS (EI) 100 (100), 69 (61).

5-Methylpyrazolidin-3-one (9):[16] 69% yield; viscous oil; IR (neat) 3210, 2973, 1684, 1344 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.28 (d, J = 6.3 Hz, 3 H), 2.18 (m, 1 H), 2.54 (dd, J = 7.0, 16.2 Hz, 1 H), 3.81 (m, 1 H), 4.10 (br s, 1 H), 7.45 (br s, 1 H): MS (EI) 100 (66), 98 (100), 89 (32), 71 (57).

4,5-Dimethylpyrazolidin-3-one (10):[16] 83% yield; 10:7 mixture of syn and anti isomers as determined by ^1H NMR; viscous oil; IR (neat) 3211, 2972, 1696, 1686 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.10-1.20(3 sets of d, 9 H), 1.32 (d, J = 7.4 Hz, 3 H), 2.20 (m, 1 H), 2.65 (quint, 1 H), 3.29 (sext, 1 H), 3.88 (quint, 1 H), 4.35 (br s, 4 H); MS (EI) 114 (100), 99 (34), 83 (24).

General Procedure for the Preparation of Pyrazolidin-3-ones by Condensation of α,β-Unsaturated Carboxylic Esters with Hydrazine Hydrate. As a typical example, the condensation of ethyl acrylate with hydrazine hydrate was carried out in the following manner. **Pyrazolidin-3-one (11).**[16] To a solution of hydrazine hydrate (6.67 mL, 0.14 mmol) in 75 mL of absolute ethanol was added ethyl acrylate (13.53 mL, 0.125 mmol) in 50 mL of absolute ethanol by dropwise addition from an addition funnel. The resulting solution was stirred for 1 h at ambient temperature and then at reflux for 4 h. The resulting solution was concentrated in vacuo to a viscous oil. Purification by column chromatography on silica gel with 15% methanol–chloroform as the elutant furnished 2.56 g (24%) of **11** as a viscous oil: IR (neat) 3389, 3223, 1680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.49 (t, J = 7.7 Hz, 2 H), 3.50 (t, J = 7.7 Hz, 2 H), 7.50 (br s, 2 H).

5-[(Ethoxycarbonyl)methyl]pyrazolidin-3-one (12): 85% yield; viscous oil; IR (neat) 3225, 1729, 1694, 1199 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.26 (t, J = 7.2 Hz, 3 H), 2.22 (dd, J = 5.5, 14.2 Hz, 1 H), 2.53 (dd, J = 5.5, 15.8 Hz, 1 H), 2.70 (m, 2 H) 4.08 (m, 1 H), 4.14 (q, J = 7.2 Hz, 2 H), 7.80 (br s, 2 H); ^{13}C NMR ($CDCl_3$) δ 14.1, 37.0, 38.1, 54.6, 60.9, 170.7, 176.2; MS (EI) 172 (23), 141 (4), 126 (15), 113 (5), 98 (16), 91 (20), 85 (100); HRMS m/z calcd for $C_7H_{12}N_2O_3$ (M^+) 172.0848, found 172.0849.

5,5-Dimethylpyrazolidin-3-one (13): 78% yield; viscous oil; bp 80–83 °C (0.1 mm) [lit.[16] bp 115° (2 mm)]; IR (neat) 3212, 2970, 1684 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.37 (s, 6 H), 2.32 (s, 2 H), 5.30 (br s, 2 H); MS (EI) 114 (74), 99 (100), 85 (65).

General Procedure for N-1 Acylation of Pyrazolidin-3-ones. As a typical example, the acylation of 4,5-dimethylpyrazolidin-3-one **10** with 2,2,2-trichloroethyl chloroformate was carried out in the following manner. **4,5-Dimethyl-1-(2,2,2-trichloroethoxycarbonyl)pyrazolidin-3-one (14).** To a solution of **10** (2.00 g, 17.5 mmol) in 10 mL of THF at 0 °C was added 10 mL of 2 N NaOH followed by dropwise addition of 2,2,2-trichloroethyl chloroformate (2.78 mL, 20.2 mmol) with vigorous stirring. The reaction mixture was warmed to ambient temperature and stirred for 3 h. The precipitate that formed during the reaction was filtered and rinsed with cold ether. Purification by column chromatography on silica gel with 10% methanol–chloroform as the elutant gave 2.87 g (57%) of **14** as a white solid: mp 126.5–128 °C (EtOH): IR (film) 3203, 1735, 1718, 1389, 1128, 712 cm^{-1}; ^1H NMR ($CDCl_3$), 10:7 mixture of syn and anti isomers, δ 1.18 (d, J = 6.8 Hz, 3 H), 1.30 (d, J = 6.4 Hz, 3 H), 1.35 (d, J = 6.8 Hz, 3 H), 1.51 (d, J = 6.4 Hz, 3 H), 2.40 (m, 1 H), 3.05 (m, 1 H), 4.12 (m, 2 H), 4.82 (s, 4 H), 8.49 (br s, 2 H); MS (EI) 288 (11), 183 (1), 156 (15), 131 (2), 114 (75), 99 (100).

5,5-Dimethyl-1-(2,2,2-trichloroethoxycarbonyl)-pyrazolidin-3-one (17): 58% yield; white needles; mp 210–212 °C [lit.[13] mp 212–212.5 °C]; IR (neat) 3176, 1703, 1397, 1381, 1339, 1284, 1170, 1130, 1110, 712 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.55 (s, 6 H), 2.70 (s, 2 H), 4.85 (s, 2 H), 4.87 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 26.2, 46.9, 62.5, 75.1, 94.8, 149.5, 167.5; MS (EI) 288 (17), 253 (3), 141 (21), 113 (56), 99 (32), 95 (20), 91 (22), 83 (100); HRMS m/z calcd for $C_8H_{11}Cl_3N_2O_3$ (M^+) 287.9837, found 287.9836.

1-(Benzyloxycarbonyl)-5,5-dimethylpyrazolidin-3-one (19). In a similar manner to that described previously for **14**, N-1 acylation of **13** was accomplished using benzyl chloroformate: 48% yield; mp 136–137 °C (ether–hexane); IR (film) 3170, 2969, 1696, 1407, 1345, 1286, 1101, 694 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.26 (br s, 1 H), 1.55 (s, 6 H), 2.65 (s, 2 H), 5.20 (s, 2 H), 7.39 (s, 5 H): ^{13}C NMR ($CDCl_3$) δ 26.0, 46.8, 62.1, 67.9, 128.3, 128.5, 128.7 (two coincident peaks), 135.4, 167.2; MS (EI) 249 (33), 234 (18), 136 (50), 120 (49), 113 (100), 91 (61); HRMS m/z calcd for $C_{13}H_{16}N_2O_3$ (M^+) 248.1161, found 248.1161.

2-Acetyl-4,5-dimethyl-1-(2,2,2-trichloroethoxycarbonyl)-pyrazolidin-3-one (15). In a similar manner to that described for the acetylation of **33**, N-2 acylation of **14** was accomplished in 61% yield: pale yellow oil; IR (neat) 1760, 1735, 1733, 1388, 1373, 1250, 1212, 1128, 715 cm^{-1}; ^1H NMR ($CDCl_3$), 10:7 mixture of syn and anti isomers, δ 1.18 (d, J = 7.7 Hz, 3 H), 1.23 (d, J = 6.5 Hz, 3 H), 1.34 (d, J = 7.9 Hz, 3 H), 1.37 (d, J = 6.7 Hz, 3 H), 2.48 (quint, 1 H), 2.55 (s, 3 H), 2.56 (s, 3 H), 3.08 (quint, 1 H), 4.39 (m, 1 H), 4.86 (m, 5 H): MS (EI) 331 (27), 288 (100), 273 (34), 253 (17), 131 (35), 113 (73), 99 (45), 83 (59).

General Procedure for the Reduction of 1-(2,2,2-Trichloroethoxycarbonyl)pyrazolidin-3-ones. As a typical example, the reduction of **15** with zinc and acetic acid was carried out in the following manner. **2-Acetyl-4,5-dimethylpyrazolidin-3-one (16).** To a solution of **15** (0.55 g 1.66 mmol) in 5 mL of acetic acid at 0 °C was added zinc dust (0.50 g, 7.69 mmol) with stirring. The reaction mixture was warmed to ambient temperature and stirred for 2 h. The crude reaction mixture was poured into 15 mL of cold saturated potassium carbonate, extracted with chloroform, washed with brine, and dried over $MgSO_4$. Filtration followed by concentration in vacuo provided an oil. Purification by column chromatography on silica gel with 5% methanol–chloroform as the elutant furnished 156 mg (60%) of

16 as a yellow oil: IR (neat) 3236, 1748, 1701, 1284 cm^{-1}; ^1H NMR ($CDCl_3$), 10:7 mixture of syn and anti isomers, δ 1.20 (3 sets of d, 9 H), 1.38 (d, J = 6.2 Hz, 3 H), 2.45 (quint, 1 H), 2.52 (s, 3 H), 2.53 (s, 3 H), 2.94 (quint, 1 H), 3.22 (quint, 1 H), 3.82 (quint, 1 H), 4.30 (br s, 2 H); MS (EI) 156 (9), 114 (57), 99 (100).

2-(*tert*-Butoxycarbonyl)-5,5-dimethylpyrazolidin-3-one (21): 27% yield; mp 97–98 °C (ether–hexane); IR (film) 1781, 1728, 1313, 1161, 1146 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.30 (s, 6 H), 1.52 (s, 9 H), 2.49 (s, 2 H), 4.48 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 25.9, 28.0, 47.6, 55.2, 83.7, 148.9, 172.1; MS (EI) 214 (1), 141 (8), 114 (75), 99 (100); HRMS m/z calcd for $C_{10}H_{18}N_2O_3$(M^+) 214.1318, found 214.1317.

Compound **21** was also prepared from **20** in a similar manner to that described for the catalytic hydrogenation of **41** to **57** in 96% yield.

2-(*tert*-Butoxycarbonyl)-5,5-dimethyl-1-(2,2,2-trichloroethoxycarbonyl)pyrazolidin-3-one (18). In a similar manner to that described for the preparation of **28**, **18** was obtained from **17** in 75% yield as off-white needles: mp 86–87 °C (ether–hexane); IR (film) 1801, 1756, 1735, 1297, 1259, 1151 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.52 (s, 9 H), 1.57 (s, 6 H), 2.62 (s, 2 H), 4.79 (s, 2 H): ^{13}C NMR ($CDCl_3$) δ 26.0, 28.0, 47.5, 64.0, 75.4, 85.0, 94.3, 148.6, 151.9, 168.8; MS (EI) 290 (38), 275 (31), 253 (5), 99 (17), 57 (100); HRMS m/z calcd for $C_{13}H_{19}Cl_3N_2O_5$ (M^+) 388.0362, (M + 1) found 389.0438.

1-(Benzyloxycarbonyl)-2-(*tert*-butoxycarbonyl)-5,5-dimethylpyrazolidin-3-one (20). In a similar manner to that described for the preparation of **28**, **20** was obtained from **19** in 91% yield as a colorless oil: IR (neat) 1798, 1770, 1750, 1725, 1298, 1274, 1258, 1151 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.44 (s, 9 H), 1.52 (s, 6 H), 2.60 (s, 2 H), 5.18 (s, 2 H), 7.37 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 26.1, 27.8, 47.8, 63.5, 68.1, 84.4, 128.5, 128.6, 128.7, 135.2, 147.8, 154.1, 169.6; MS (EI) 249 (24), 232 (82), 136 (28), 113 (20), 99 (14), 78 (17), 57 (100); HRMS m/z calcd for $C_{18}H_{24}N_2O_5$ (M^+) 348.1686, (M + 1) found 349.1533.

General Procedure for the Preparation of 1-(*o*-Nitrobenzyl)pyrazolidin-3-ones. As a typical example, the benzylation of 4-methylpyrazolidin-3-one **8** was carried out in the following manner. **4-Methyl-1-(*o*-nitrobenzyl)pyrazolidin-3-one (22).** To a solution of **8** (1.81 g, 18.1 mmol) in 20 mL of DMF was added triethylamine (2.52 mL, 18.1 mmol), *o*-nitrobenzyl chloride (2.59 g, 15.1 mmol), and sodium iodide (0.68 g, 4.53 mmol). The resulting mixture was stirred at ambient temperature under argon for 48 h. The reaction mixture was concentrated under high vacuum, and the residue was partitioned between chloroform and water. The aqueous layer was extracted twice with chloroform and the organic layers were combined, washed with brine, and dried over $MgSO_4$. Filtration followed by concentration in vacuo provided an oil. Purification by column chromatography on silica gel with 6% methanol–chloroform as the elutant gave an oil which was triturated with methylene chloride–ether to afford 2.67 g (63%) of **22** as an orange colored solid: mp 108–109 °C; IR (film) 3202, 2934, 1695, 1528, 1355 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.18 (d, J = 8.7 Hz, 3 H), 2.85 (m, 1 H), 3.01 (m, 1 H), 3.48 (dd, J = 7.9, 12.6 Hz, 1 H), 4.23 (s, 2 H), 7.00 (br s, 1 H), 7.45 (m, 1 H), 7.60 (d, J = 6.3 Hz, 2 H), 7.84 (d, J = 9.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 13.5, 34.8, 60.2, 60.4, 124.9, 128.8, 131.0, 131.6, 133.2, 149.2, 177.3; MS (EI) 234 (40), 217 (17), 137 (17), 120 (100), 99 (95); HRMS m/z calcd for $C_{11}H_{13}N_3O_3$ (M^+) 235.0957, found 235.0953.

5-Methyl-1-(*o*-nitrobenzyl)pyrazolidin-3-one (23): 56% yield; orange colored oil; IR (neat) 3184, 3072, 2974, 1694, 1522, 1346 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.23 (d, J = 6.6 Hz, 3 H), 2.06 (dd, J = 5.5, 16.9, 1 H), 2.77 (dd, J = 7.7, 16.7 Hz, 1 H), 3.38 (sext, 1 H), 4.03 (d, J = 14.0 Hz, 1 H), 4.43 (d, J = 14.0 Hz, 1 H), 7.10 (br s, 1 H), 7.48 (m, 1 H), 7.60 (d, J = 3.9 Hz, 2 H), 7.92 (d, J = 8.2 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 19.6, 36.6, 59.4, 59.6, 125.0, 129.0, 131.1, 131.3, 133.2, 149.4, 174.2; MS (EI) 235 (15), 218 (24), 136 (31), 120 (12), 99 (100); HRMS m/z calcd for $C_{11}H_{13}N_3O_3$ (M^+) 235.0957, found 235.0958.

4,5-Dimethyl-1-(*o*-nitrobenzyl)pyrazolidin-3-one (24): 71% yield; 10:7 mixture of syn and anti isomers as determined by ^1H NMR; yellow needles; mp 133–134 °C (CH_2Cl_2–ether); IR (KBr) 3158, 2972, 1698, 1523, 1348 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.09 (2 sets of d, J = 6.9 and 7.4 Hz, 6 H), 1.19 (d, J = 7.1 Hz, 3 H), 1.33 (d, J = 6.2 Hz, 3 H), 2.25 (m, 1 H), 2.81 (sext, 1 H), 3.02 (quint, 1 H), 3.46 (quint, 1 H), 3.77 (d, J = 14.1 Hz, 1 H), 4.11 (d, J = 13.9 Hz, 1 H), 4.49 (d, J = 13.9 Hz, 1 H), 4.59 (d, 14.1 Hz, 1 H), 7.48 (m, 2 H), 7.61 (m, 4 H), 7.94 (2 sets of d, J = 7.8 and 7.9 Hz, 2 H); MS (EI) 249 (18), 232 (10), 202 (2), 136 (20), 120 (59), 113 (100); HRMS m/z calcd for $C_{12}H_{15}N_3O_3$ (M^+) 249.1114, found 249.1113.

1-(*o*-Nitrobenzyl)pyrazolidin-3-one (25): 65% yield; yellow prisms, mp 100–101 °C (hexane–ethyl acetate): IR (KBr) 3421, 1685, 1524, 1359, 1343, 731 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.56 (t, J = 7.8 Hz, 2 H), 3.37 (t, J = 7.8 Hz, 2 H), 4.24 (s, 2 H), 7.24 (s, 1 H), 7.48 (m, 1 H), 7.62 (m, 2 H), 7.94 (d, J = 7.8 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 29.7, 52.3, 60.1, 124.8, 128.7, 131.0, 131.4, 133.2, 149.1, 175.1; MS (EI) 221 (24), 204 (16), 137 (32), 121 (1), 120 (100), 92 (65), 85 (78); HRMS m/z calcd for $C_{10}H_{11}N_3O_3$ (M^+) 221.0801, found 221.0799.

5-[(Ethoxycarbonyl)methyl]-1-(*o*-nitrobenzyl)-pyrazolidin-3-one (26): 32% yield; pale yellow oil; IR (neat) 3189, 2984, 1730, 1694, 1529, 1354, 1191 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.21 (t, J = 7.2 Hz, 3 H), 2.04 (dd, J = 2.8, 17.2 Hz, 1 H), 2.37 (dd, J = 6.8, 16.0 Hz, 1 H), 2.61 (dd, J = 7.7, 15.9 Hz, 1 H), 2.99 (dd, J = 8.2, 17.1 Hz, 1 H), 3.73 (m, 1 H), 4.10 (m, 3 H), 4.36 (d, J = 13.7 Hz, 1 H), 7.40–7.60 (m, 3 H), 7.87 (dd, J = 0.9, 8.0 Hz, 1 H), 7.97 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.0, 34.2, 39.3, 59.7, 60.2, 60.7, 124.8, 128.9, 131.0, 131.3, 133.0, 149.4, 170.5, 174.0; MS (EI) 307 (18), 290 (9), 220 (52), 189 (7), 172 (28), 136 (84), 125 (43), 120 (93), 97 (95), 91 (100); HRMS m/z calcd for $C_{14}H_{17}N_3O_5$ (M^+) 307.1169, found 307.1170.

General Procedure for the Acetylation of 1-(*o*-Nitrobenzyl)pyrazolidin-3-ones. As a typical example, the acetylation of 5-methyl-1-(*o*-nitrobenzyl)pyrazolidin-3-one (**23**) was carried out in the following manner. **2-Acetyl-5-methyl-1-(*o*-nitrobenzyl)pyrazolidin-3-one (33).** To a solution of **23** (245 mg, 1.04 mmol) in 18 mL of dry THF at 0 °C was added triethylamine (160 μL, 1.15 mmol) followed by acetyl chloride (82 μL, 1.15 mmol) with vigorous stirring under argon. After 6 h, the reaction mixture was diluted with ether, and the salts were removed by filtration. Concentration of the solution in vacuo provided a mixture of O- and N-acylation products as determined by ^1H NMR and IR. The crude reaction mixture was subjected to thermolysis at 110 °C for 6 h under argon. The product was then purified by column chromatography on silica gel with 1:1 hexane–ethyl acetate as the elutant to afford 235 mg (82%) of **33** as a pale yellow oil: IR (neat) 1747, 1707, 1523, 1370, 1348, 1277, 1247, 730 cm^{-1}; ^{H} NMR ($CDCl_3$) δ 1.16 (d, J = 6.7 Hz, 3 H), 2.25 (d, J = 17.1 Hz, 1 H), 2.50 (s, 3 H), 3.24 (dd, J = 7.8, 17.1 Hz, 1 H), 3.36 (m, 1 H), 4.27 (d, J = 14.4 Hz, 1 H), 4.35 (d, J = 14.4 Hz, 1 H), 7.49 (m, 1 H), 7.66 (m, 1 H), 7.93 (m, 1 H), 8.06 (d, J = 7.8 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 20.7, 24.4, 37.3, 53.8, 55.2, 124.4, 128.5, 131.5, 131.6, 133.3, 149.0, 167.0, 173.4; MS (EI) 277 (1), 235 (100), 218 (82), 187 (10), 146 (43), 136 (26), 120 (62), 99 (62): HRMS m/z calcd for $C_{13}H_{15}N_3O_4$ (M^+) 277.1063, found 277.1062.

2-Acetyl-4-methyl-1-(*o*-nitrobenzyl)pyrazolidin-3-one (27): 77% yield; white prisms; mp 133–134 °C (CH_2Cl_2–ether); IR (film) 1747, 1707, 1528, 1281, 1216, 754, 669 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.22 (d, J = 6.5 Hz, 3 H), 2.52 (s, 3 H), 3.10 (m, 2 H), 3.37 (dd, J = 7.2, 11.1 Hz, 1 H), 4.28 (d, J = 14.1 Hz, 1 H), 4.43 (d, J = 14.1 Hz, 1 H), 7.47 (m, 1 H), 7.66 (m, 1 H), 7.93 (m, 1 H), 8.03 (d, J = 7.8 Hz, 1 H): ^{13}C NMR ($CDCl_3$) δ 13.0, 24.5, 35.4, (two coincident peaks), 124.4, 128.6, 131.4, 132.0, 133.4, 149.1, 166.8, 176.1; MS (EI) 277 (2), 235 (100), 218 (63), 173 (3), 146 (9), 137 (15), 120 (55), 99 (39); HRMS m/z calcd for $C_{13}H_{15}N_3O_4$ (M^+) 277.1063, found 277.1063.

General Procedure for the Preparation of 2-(*tert*-Butoxycarbonyl)pyrazolidin-3-ones. As a typical example, the t-BOC substituent was introduced at N-2 of 4-methyl-1-(*o*-nitrobenzyl)pyrazolidin-3-one (**22**) with di-*tert*-butyl dicarbonate in the following manner. **2-(*tert*-Butoxycarbonyl)-4-methyl-1-(*o*-nitrobenzyl)pyrazolidin-3-one (28).** To a solution of **22** (253 mg, 1.08 mmol) in 10 mL of CH_2Cl_2 was added triethylamine (0.17 mL, 1.19 mmol), DMAP (146 mg, 1.19 mmol), and di-*tert*-butyl dicarbonate (471 mg, 2.16 mmol) with stirring under argon. After stirring for 3 h at ambient temperature, the resulting solution was partitioned between CH_2Cl_2 and water. The aqueous layer was extracted with CH_2Cl_2, and the organic layers were washed with brine and dried over $MgSO_4$. Filtration followed by concentration in vacuo resulted in an oil. Purification by column chromatography on silica gel with 1:1 hexane–ethyl acetate as the elutant gave 355 mg (98%) of **28** as a colorless oil: IR (neat)

1785, 1734, 1527, 1301 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.17 (d, J = 7.1 Hz, 3 H), 1.52 (s, 9 H), 3.03 (m, 2 H), 3.30 (sext, 1 H), 4.26 (d, J = 15.0 Hz, 1 H), 4.49 (d, J = 15.0 Hz, 1 H), 7.46 (t, J = 7.8 Hz, 1 H), 7.65 (dt, J = 1.6, 7.8 Hz, 1 H), 7.94 (m, 2 H); ^{13}C NMR ($CDCl_3$) 13.1, 35.1, 55.7, 56.0, 83.9, 124.5, 128.6, 131.6, 131.8, 133.3, 148.4, 149.2, 174.5; MS (EI) 335 (0.5), 286 (3), 234 (32), 217 (43), 137 (12), 120 (25); HRMS m/z calcd for $C_{16}H_{21}N_3O_5$ (M^+ 335.1482, found 335.1487.

2-(*tert*-Butoxycarbonyl)-5-methyl-1-(*o*-nitrobenzyl)-pyrazolidin-3-one (34): 96% yield; colorless crystals; mp 90–91.5 °C (ether–hexane); IR (film) 1781, 1732, 1528, 1301, 1251, 1146 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.18 (d, J = 6.7 Hz, 3 H), 1.50 (s, 9 H), 2.17 (d, J = 17.8 Hz, 1 H), 3.18 (dd, J = 7.6, 17.3 Hz, 1 H), 3.30 (sept, 1 H), 4.25 (d, J = 14.5 Hz, 1 H), 4.40 (d, J = 14.5 Hz, 1 H), 7.46 (dt, J = 1.1, 7.6 Hz, 1 H), 7.63 (dt, J = 1.1, 7.7 Hz, 1 H), 7.95 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 20.5, 28.0, 37.2, 54.6, 56.3, 83.8, 124.6, 128.5, 131.3, 131.9, 133.2, 148.8, 149.1, 172.1; MS (EI) 337 (2), 235 (63), 218 (49), 146 (13), 136 (20), 120 (64), 100 (100); HRMS m/z calcd for $C_{16}H_{21}N_3O_5$ (M^+) 335.1481, (M + 1) found 336.1559.

2-(*tert*-Butoxycarbonyl)-4,5-dimethyl-1-(*o*-nitrobenzyl)-pyrazolidin-3-one (35): 99% yield, 10:7 mixture of syn and anti isomers as determined by ^{1}H NMR; colorless oil; IR (neat) 1780, 1733, 1522, 1307, 1282, 1253 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.05 (d, J = 6.7 Hz, 3 H), 1.10 (d, J = 7.0 Hz, 3 H), 1.16 (d, J = 6.8 Hz, 3 H), 1.27 (d, J = 7.3 Hz, 3 H), 1.41 (s, 9 H), 1.49 (s, 9 H), 2.53 (quint, 1 H), 3.21 (m, 2 H), 2.32 (m, 1 H), 4.13 (d, J = 14.8 Hz, 1 H), 4.21 (d, J = 14.6 Hz, 1 H), 4.53 (d, J = 14.6 Hz, 1 H), 4.69 (d, J = 14.8 Hz, 1 H), 7.43 (m, 2 H), 7.62 (m, 2 H), 7.97 (m, 4 H); MS (EI) 249 (1), 147 (15), 137 (50), 121 (72), 114 (81), 92 (33), 78 (100); HRMS m/z calcd for $C_{17}H_{23}N_3O_5$ (M^+) 349.1638, (M + 1) found 350.1716.

2-(*tert*-Butoxycarbonyl)-5-[(ethoxycarbonyl)methyl]-1-(*o*-nitrobenzyl)pyrazolidin-3-one (38): 94% yield; amber oil; IR (neat) 1786, 1735, 1528, 1369, 1351, 1298, 1256, 1161 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.19 (t, J = 7.2 Hz, 3 H) 1.48 (s, 9 H), 2.35 (d, J = 17.4 Hz, 1 H) 2.43 (dd, J = 7.7, 15.8 Hz, 1 H) 2.60 (dd, J = 6.9, 15.8 Hz, 1 H), 3.27 (dd, J = 7.7, 17.4 Hz, 1 H), 3.70 (q, 1 H), 4.06 (m, 2 H), 4.18 (d, J = 13.9 Hz, 1 H), 4.50 (d, J = 13.9 Hz, 1 H), 7.47 (m, 1 H), 7.62 (m, 1 H), 7.85 (d, J = 7.1 Hz, 1 H), 7.94 (d, J = 7.1 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.0, 27.9, 35.6, 39.2, 55.8, 56.6, 60.8, 83.9, 124.6, 128.8, 130.9, 132.0, 133.0, 148.4, 149.3, 170.0, 171.5; MS (EI) 307 (79), 290 (22), 262 (10), 220 (58), 199 (18), 172 (72), 136 (97), 120 (100); HRMS m/z calcd for $C_{19}H_{25}N_3O_7$ (M^+) 407.1693, found 407.1693.

2-(Benzyloxycarbonyl)-4-methyl-1-(*o*-nitrobenzyl)-pyrazolidin-3-one (29). To a solution of **22** (340 mg, 1.45 mmol) in 25 mL of dry THF at 0 °C was added triethylamine (0.72 mL, 5.22 mmol) and benzyl chloroformate (0.75 mL, 5.22 mmol) with stirring under argon. The reaction mixture was warmed to ambient temperature and then stirred overnight. The mixture was filtered to remove the salts and concentrated in vacuo to give an oil. Purification by column chromatography on silica gel with 2:1 hexane–ethyl acetate as the elutant afforded 306 mg (57%) of the O-acylated product and 90 mg (17%) of the desired N-acylated product as determined by ^{1}H NMR and IR. A portion (303 mg, 0.82 mmol) of the O-acylated product was subjected to thermolysis at 110 °C under argon for 9 h to yield 300 mg (99%) of **29** as a pale yellow oil: combined yield 73%; IR (neat) 1789, 1759, 1734, 1523, 1349, 1287, 1214, 1131 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.21 (d, J = 6.4 Hz, 3 H), 3.09 (m, 2 H), 3.45 (m, 1 H), 4.25 (d, J = 13.9 Hz, 1 H), 4.48 (d, J = 13.9 Hz, 1 H), 5.27 (s, 2 H), 7.38 (m, 6 H), 7.57 (m, 1 H), 7.80 (m, 1 H), 7.90 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 12.9, 34.8, 55.8, 56.2, 68.3, 124.3, 128.2, 128.3, 128.4, 128.6, 131.0, 131.7, 133.1, 134.8, 149.1, 149.6, 174.5; MS (EI) 369 (0.1), 325 (2), 234 (29), 189 (21), 136 (15), 99 (13), 91 (100); HRMS m/z calcd for $C_{19}H_{19}N_3O_5$ (M^+) 369.1326, found 369.1326.

2-(Ethoxycarbonyl)-5-methyl-1-(*o*-nitrobenzyl)-pyrazolidin-3-one (32). In a manner similar to that described for the preparation of **29**, **32** was obtained by treatment of **23** (180 mg, 0.77 mmol) with triethylamine (117 μL, 0.84 mmol) and ethyl chloroformate (81 μL, 0.84 mmol). Purification by column chromatography on silica gel with 1:1 hexane–ethyl acetate as the elutant gave 172 mg (73%) of **32** as a yellow oil: IR (neat) 1788, 1738, 1527, 1369, 1351, 1288, 1253 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.28 (d, J = 6.4 Hz, 3 H), 1.39 (t, J = 6.4 Hz, 3 H), 2.22 (d, J = 17.4 Hz, 1 H), 3.30 (dd, J = 6.4, 17.4 Hz, 1 H), 3.48 (m, 1 H), 4.28 (m, 3 H), 4.42 (d, J = 14.2 Hz, 1 H), 7.48 (m, 1 H), 7.63 (m, 1 H), 7.81 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 14.0, 17.6, 38.4, 55.2, 64.5, 65.3, 124.5, 127.9, 131.6, 133.0, 133.6, 148.9, 151.4, 155.6; MS (EI) 234 (25), 187 (9), 146 (17), 136 (40), 120 (21), 99 (16), 78 (100); HRMS m/z calcd for $C_{14}H_{17}N_3O_5$ (M^+) 307.1169, found 307.1169.

General Procedure for the Preparation of 1-[2-(Trimethylsilyl)ethoxycarbonyl]pyrazolidin-3-ones. As a typical example, the (trimethylsilyl)ethoxycarbonyl substituent was introduced at N-2 of 4-methyl-1-(*o*-nitrobenzyl)pyrazolidin-3-one (**22**) with 2-(trimethylsilyl)ethyl azidoformate in the following manner. **4-Methyl-1-(*o*-nitrobenzyl)-2-[2-(trimethylsilyl)-ethoxycarbonyl]pyrazolidin-3-one (30).** To a suspension of sodium hydride (90 mg of a 60% dispersion, 2.25 mmol) in 15 mL of dry THF at 0 °C under argon was added **22** (350 mg, 1.79 mmol) dropwise as a solution in 5 mL of THF. The resulting solution was stirred for 45 min then treated with a solution of 2-(trimethylsilyl)ethyl azidoformate[19] (335 mg, 1.79 mmol) in 5 mL of THF. The mixture was stirred at 0 °C for 30 min and for 1.5 h at ambient temperature. The resulting mixture was partitioned between ethyl acetate and water. The aqueous layer was extracted three times with ethyl acetate, and the organic layers were combined, washed with brine, and dried over $MgSO_4$. Filtration followed by concentration in vacuo yielded an oil. Purification by column chromatography on silica gel with 2.5:1 hexane–ethyl acetate as the elutant gave a white solid. Trituration with ether–hexane gave 412 mg (73%) of **30** as white prisms: mp 110–111 °C; IR (film) 1749, 1721, 1529, 1357, 1292, 1250, 859, 840, 756 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.40 (s, 9 H), 1.09 (t, J = 8.7 Hz, 2 H), 1.20 (d, J = 6.4 Hz, 3 H), 3.08 (m, 2 H), 3.35 (m, 1 H), 4.29 (m, 3 H), 4.48 (d, J = 13.4 Hz, 1 H), 7.47 (m, 1 H), 7.62 (m, 1 H), 7.91 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ −1.7, 13.0, 17.4, 35.0, 55.9, 56.2, 65.7, 124.4, 128.6, 131.2, 131.8, 133.2, 149.2, 150.0, 174.4; MS (EI) 380 (63), 352 (99), 308 (100), 290 (70), 171 (20); HRMS m/z calcd for $C_{17}H_{25}N_3O_5Si$ (M^+) 379.1564, found 379.1565. Anal. Calcd for $C_{17}H_{25}N_3O_5Si$: C, 53.80; H, 6.65; N, 11.08. Found: C, 53.81; H, 6.77; N, 11.11.

5-Methyl-1-(*o*-nitrobenzyl)-2-[2-(trimethylsilyl)ethoxycarbonyl]pyrazolidin-3-one (31): 81% yield; white crystals; mp 103–104 °C (hexane–ethyl acetate); IR (film) 1789, 1737, 1528, 1383, 1350, 1286, 1251, 859, 839 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.04 (s, 9 H), 1.07 (t, J = 8.7 Hz, 2 H), 1.18 (d, J = 6.6 Hz, 3 H), 2.20 (d, J = 17.6 Hz, 1 H), 3.18 (dd, J = 7.0, 17.4 Hz, 1 H), 3.35 (m, 1 H), 4.28 (m, 3 H), 4.41 (d, J = 14.1 Hz, 1 H), 7.46 (t, J = 7.6 Hz, 1 H), 7.64 (t, J = 7.5 Hz, 1 H), 7.92 (m, 2 H): ^{13}C NMR ($CDCl_3$) δ −1.9, 17.1, 20.2, 36.7, 54.5, 56.3, 65.2, 124.2, 128.3, 131.1, 131.3, 132.9, 148.9, 150.0, 171.8; MS (EI) 379 (0.1), 307 (4), 290 (25), 171 (5), 136 (8), 120 (8), 101 (10), 73 (100); HRMS m/z calcd for $C_{17}H_{25}N_3O_5Si$ (M^+) 379.1564, found 379.1565. Anal. Calcd for $C_{17}H_{25}N_3O_5Si$: C, 53.80; H, 6.65; N, 11.08. Found: C, 53.98; H, 6.76; N, 11.19.

***cis*-4,5-Dimethyl-1-(*o*-nitrobenzyl)-2-[2-(trimethylsilyl)-ethoxycarbonyl]pyrazolidin-3-one (36) and *trans*-4,5-Dimethyl-1-(*o*-nitrobenzyl)-2-[2-(trimethylsilyl)ethoxycarbonyl]pyrazolidin-3-one (36)**: 59% combined yield; *cis*-**36**: 32% yield; white prisms; mp 101–102.5 °C (ether–hexane); IR (neat) 2955, 1789, 1762, 1734, 1530, 1282, 861, 838, 766 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.04 (s, 9 H), 1.07 (m, 8 H). 3.26 (quint, 1 H), 3.38 (quint, 1 H), 4.26 (m, 3 H), 4.54 (d, J = 14.4 Hz, 1 H), 7.46 (t, J = 7.6 Hz, 1 H), 7.64 (t, J = 7.5 Hz, 1 H), 7.95 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ −1.6, 9.4, 15.4, 17.5, 38.2, 55.8, 59.1, 65.6, 124.5, 128.5, 131.4, 131.9, 133.2, 149.2, 150.5, 174.2; MS (CI) 393 (35), 366 (38), 350 (47), 321 (70), 157 (35), 133 (100); HRMS m/z calcd for $C_{18}H_{27}N_3O_5Si$ (M^+) 393.1721, found 393.1721. Anal. Calcd for $C_{18}H_{27}N_3O_5Si$: C, 54.94; H, 6.92; N, 10.69. Found: C, 54.77; H, 6.92; N, 10.65. *trans*-**36**: 27% yield; yellow oil; IR (neat) 2955, 1787, 1762, 1737, 1529, 1390, 1353, 1281, 861, 763 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.01 (s, 9 H), 0.96 (t, J = 8.8 Hz, 2 H), 1.19 (t, J = 6.8 Hz, 3 H), 1.29 (t, J = 7.2 Hz, 3 H), 2.54 (quint, 1 H), 3.24 (quint, 1 H), 4.15 (m, 3 H), 4.73 (d, J = 14.5 Hz, 1 H), 7.45 (t, J = 7.5 Hz, 1 H), 7.60 (t, J = 7.5 Hz, 1 H), 7.92 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ −1.8, 13.8, 17.2 (two coincident peaks), 43.0, 55.3, 63.5, 65.5, 124.4, 128.4, 131.8, 132.2, 132.8, 149.0, 150.1, 174.9; MS (CI) 393 (10), 366 (18), 350 (20), 321 (52), 157 (12), 133 (100); HRMS m/z calcd for $C_{18}H_{27}N_3O_5Si$ (M^+) 393.1721, found 393.1721. Anal. Calcd for $C_{18}H_{27}N_3O_5Si$: C, 54.94; H, 6.92, N, 10.69. Found: C, 54.91; H, 6.94; N, 10.53.

1-(*o*-Nitrobenzyl)-2-[2-(trimethylsilyl)ethoxycarbonyl]-pyrazolidin-3-one (37): 90% yield; white prisms; mp 98–99 °C (hexane–ethyl acetate); IR (neat) 2954, 1789, 1734, 1528, 1382, 1289, 861, 839 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.05 (s, 9 H), 1.10 (t, J = 9.2 Hz, 2 H), 2.80 (m, 2 H), 3.33 (t, J = 7.4 Hz, 2 H), 4.33 (t, J = 9.4 Hz, 2 H), 4.37 (s, 2 H), 7.48 (m, 1 H), 7.65 (m, 1 H), 7.88 (d, J = 7.7 Hz, 1 H), 7.94 (d, J = 7.2 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ −1.8, 17.4, 30.4, 48.0, 56.0, 65.7, 124.4, 128.6, 130.9, 131.8, 133.1, 149.2, 149.7, 172.0; MS (CI) 366 (2), 338 (86), 294 (87), 114 (97), 83 (100); HRMS m/z calcd for $C_{16}H_{23}N_3O_5Si$ (M^+) 365.1408, found 365.1405. Anal. Calcd for $C_{16}H_{23}N_3O_5Si$: C, 52.58; H, 6.36; N, 11.50. Found: C, 52.37; H, 6.24; N, 11.41.

5-[(Ethoxycarbonyl)methyl]-1-(*o*-nitrobenzyl)-2-[2-(trimethylsilyl)ethoxycarbonyl]pyrazolidin-3-one (39): 90% yield; colorless oil; IR (neat) 2956, 1789, 1736, 1529, 1287, 1251, 860, 839, 763 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.03 (s, 9 H), 1.04 (t, J = 8.5 Hz, 2 H), 1.17 (t, J = 7.2 Hz, 3 H), 2.48 (m, 2 H), 2.59 (dd, J = 7.0, 15.9 Hz, 1 H), 3.26 (dd, J = 7.8, 18.0 Hz, 1 H), 3.73 (q, J = 7.4 Hz, 1 H), 4.02 (m, 2 H), 4.22 (m, 3 H), 4.49 (d, J = 13.7 Hz, 1 H), 7.46 (m, 1 H), 7.61 (m, 1 H), 7.79 (m, 1 H), 7.90 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ −1.6, 14.0, 17.5, 35.4, 39.1, 55.8, 56.8, 60.8, 65.8, 124.5, 128.9, 130.6, 132.2, 133.0, 149.4, 150.0, 169.9, 171.2; MS (EI) 452 (22), 424 (95), 380 (100), 322 (84), 292 (50); HRMS m/z calcd for $C_{20}H_{29}N_3O_7Si$ (M^+) 451.1775, found 451.1776. Anal. Calcd for $C_{20}H_{29}N_3O_7Si$: C, 53.19; H, 6.49; N, 9.31. Found: C, 53.31; H, 6.52; N, 9.32.

General Procedure for the Tandem Photochemical Conversion of Acylpyrazolidin-3-ones to 1-(Acylamino)azetidin-2-ones. As a typical example, the photolysis of 2-(*tert*-butoxycarbonyl)-1-(*o*-nitrobenzyl)-3-methylpyrazolidin-3-one (**28**) to the corresponding 1-(acylamino)azetidin-2-one was carried out in the following manner. **1-[(*tert*-Butoxycarbonyl)amino]-3-methylazetidin-2-one (40).** A solution of **28** (537 mg, 1.60 mmol) in 150 mL of absolute ethanol was degassed with argon for 2 h in a photochemical immersion well. The solution was irradiated for 1.5 h at 0 °C through a Pyrex filter with a 450-W Hanovia medium-pressure photochemical lamp. The Pyrex filter was then replaced by a Vycor filter, and the solution was irradiated for 2.5 h at 0 °C. The resulting solution was then concentrated in vacuo to a dark brown oil. Purification by column chromatography on silica gel (loaded with 10% methanol–chloroform) with 1:1 hexane–ethyl acetate as the elutant provided 270 mg (84%) of **40** as an orange oil: IR (neat) 3296, 2979, 1774, 1729, 1249, 1163, 755 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.33 (d, J = 7.9 Hz, 3 H), 1.48 (s, 9 H), 3.10 (br t, 1 H), 3.25 (br s, 1 H), 3.70 (br s, 1 H), 6.51 (s, 1 H); MS (EI) 200 (3), 176 (4), 154 (7), 145 (45), 127 (100); HRMS m/z calcd for $C_9H_{16}N_2O_3$ (M^+) 200.1161, found 200.1161.

1-[(Benzyloxycarbonyl)amino]-3-methylazetidin-2-one (41): 17% yield; amber oil; IR (neat) 3274, 2973, 1775, 1735, 1500, 1455, 1233, 1051, 748, 699 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.35 (m, 3 H), 3.08 (m, 1 H), 3.22 (m, 1 H), 3.68 (m, 1 H), 5.12 (s, 2 H), 7.35 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 13.1, 29.6, 41.9, 52.2, 67.9, 128.4, 128.5, 135.2, 154.8, 172.2; MS (EI) 202 (1), 188 (1), 173 (2), 159 (4), 145 (4), 123 (4), 107 (6), 91 (100); MS (CI) 235 (5), 191, (16), 179 (12), 135 (9), 91 (100); HRMS m/z calcd for $C_{12}H_{14}N_2O_3$ (M^+) 234.1005, found 234.1005.

3-Methyl-1-[[2-(trimethylsilyl)ethoxycarbonyl]amino]-azetidin-2-one (42): 60% yield; yellow oil; IR (neat) 3260, 2956, 1775, 1734, 1505, 1249, 1062, 860, 839 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.04 (s, 9 H), 1.02 (t, J = 8.7 Hz, 2 H), 1.36 (d, J = 7.3 Hz, 3 H), 3.13 (m, 1 H), 3.25 (br s, 1 H), 3.72 (t, J = 4.9 Hz, 1 H), 4.24 (t, J = 8.7 Hz, 2 H), 6.61 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ −1.6, 13.2, 17.6, 18.1, 41.8, 52.2, 64.8, 155.1, 172.2; MS (CI) 245 (20), 217 (48), 201 (52), 173 (100), 157 (12); HRMS m/z calcd for $C_{10}H_{20}N_2O_3Si$ (M^+) 244.1243, found 244.1243.

4-Methyl-1-[[2-(trimethylsilyl)ethoxycarbonyl]amino]-azetidin-2-one (43): 44% yield; yellow oil; IR (neat) 3275, 2956, 1781, 1734, 1506, 1383, 1207, 1061, 1048, 861, 838, 757 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.02 (s, 9 H), 1.00 (t, J = 8.7 Hz, 2 H), 1.34 (d, J = 6.1 Hz, 3 H), 2.42 (dd, J = 1.9, 14.4 Hz, 1 H), 2.98 (dd, J = 5.0, 14.5 Hz, 1 H), 3.98 (br s, 1 H), 4.21 (t, J = 8.4 Hz, 2 H), 7.03 (br s 1 H); ^{13}C NMR ($CDCl_3$) δ −1.6, 17.6, 17.7, 41.4, 52.9, 64.8, 155.2, 168.0; MS (EI) 244 (0.3), 201 (35), 172 (10), 157 (50), 130 (39), 115 (24), 101 (62), 73 (100); HRMS m/z calcd for $C_{10}H_{20}N_2O_3Si$ (M^+) 244.1243, found 244.1243.

1-[(*tert*-Butoxycarbonyl)amino]-4-methylazetidin-2-one (44): 65% yield; orange oil; IR (neat) 3275, 2979, 1775, 1726, 1206, 1163, 756 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.36 (d, J = 6.0 Hz, 3 H), 1.47 (s, 9 H), 2.43 (dd, J = 1.9, 14.6 Hz, 1 H), 2.99 (dd, J = 4.3, 14.1 Hz, 1 H) 3.98 (br m, 1 H), 6.50 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 17.8, 28.1, 28.2, 41.3, 52.8, 82.1, 153.9, 167.9; MS (EI) 200 (1), 129 (100), 100, (61), 83 (52); HRMS m/z calcd for $C_9H_{16}N_2O_3$ (M^+) 200.1161, found 200.1161.

1-[(*tert*-Butoxycarbonyl)amino]-3,4-dimethylazetidin-2-one (45): 79% yield, 10:7 mixture of cis and trans isomers; orange oil; IR (neat) 3274, 2977, 1771, 1730, 1250, 1161, 756 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.19 (d, J = 7.5 Hz, 3 H), 1.23 (d, J = 6.4 Hz, 3 H), 1.32 (d, J = 7.0 Hz, 3 H), 1.34 (d, J = 6.1 Hz, 3 H), 1.47 (s, 9 H), 1.50 (s, 9 H), 2.62 (m, 1 H), 3.15 (m, 1 H), 3.60 (br m, 1 H), 4.04 (br m, 1 H), 6.45 (br s, 2 H); MS (EI) 215 (5), 174 (7), 159 (19), 141 (64), 114 (14), 103 (100); HRMS m/z calcd for $C_{10}H_{18}N_2O_3$ (M^+) 214.1318, found 214.1317.

***cis*-3,4-Dimethyl-1-[[2-(trimethylsilyl)ethoxycarbonyl]-amino]azetidin-2-one (46)**: 55% yield, amber oil; IR (neat) 3274, 2955, 1773, 1735, 1506, 1383, 1250, 1235, 1063, 861, 839 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.01 (s, 9 H), 0.99 (t, J = 8.8 Hz, 2 H), 1.17 (d, J = 7.5 Hz, 3 H), 1.21 (d, J = 6.4 Hz, 3 H), 3.15 (m, 1 H), 4.04 (br s, 1 H), 4.20 (t, J = 8.2 Hz, 2 H), 7.11 (br s, 1 H): ^{13}C NMR ($CDCl_3$) δ −1.6, 8.5, 12.7, 17.6, 44.3, 56.4, 64.7, 155.3, 171.6; MS (EI) 258 (0.4), 231 (2), 186 (10), 171 (42), 159 (27), 130 (43), 115 (23), 101 (68), 73 (100); HRMS m/z calcd for $C_{11}H_{22}N_2O_3Si$ (M^+) 258.1400, found 258.1399.

***trans*-3,4-Dimethyl-1-[[2-(trimethylsilyl)ethoxycarbonyl]amino]azetidin-2-one (47)**: 51% yield, amber oil; IR (neat) 3274, 2956, 1774, 1734, 1505, 1381, 1310, 1179, 1062, 861, 839 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.00 (s, 9 H), 0.98 (t, J = 8.8 Hz, 2 H), 1.28 (d, J = 8.0 Hz, 3 H), 1.31 (d, J = 6.3 Hz, 3 H), 2.60 (m, 1 H), 3.57 (br s, 1 H), 4.18 (t, J = 8.7 Hz, 2 H), 7.12 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ −1.6, 12.3, 17.0, 17.5, 49.0, 61.0, 64.7, 155.3, 171.4; MS (EI) 258 (0.4), 186 (12), 171 (43), 159 (28), 130 (32), 115 (21), 101 (70), 73 (100); HRMS m/z calcd for $C_{11}H_{22}N_2O_3Si$ (M^+) 258.1400, found 258.1399.

1-[[2-(Trimethylsilyl)ethoxycarbonyl]amino]azetidin-2-one (48): 34% yield, amber oil; IR (neat) 3200, 1786, 1735, 1505, 1250, 1062, 1045, 862, 839 cm^{-1}; ^1H NMR ($CDCl_3$) δ −0.02 (s, 9 H), 0.96 (t, J = 8.7 Hz, 2 H), 2.80 (t, J = 3.9 Hz, 2 H), 3.52 (br s, 2 H), 4.17 (t, J = 8.7 Hz, 2 H), 7.50 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ −1.7, 17.5, 34.0, 44.1, 64.6, 155.2, 168.8; MS (EI) 230 (0.2), 187 (47), 158 (19), 143 (28), 130 (3), 116 (28), 101 (75), 73 (100); HRMS m/z calcd for $C_9H_{18}N_2O_3Si$ (M^+) 230.1087, found 230.1086.

1-[(*tert*-Butoxycarbonyl)amino]-4-[(ethoxycarbonyl)-methyl]azetidin-2-one (49): 58% yield; yellow oil; IR (neat) 3305, 2981, 1787, 1734, 1370, 1271, 1251, 1181, 1162 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.27 (t, J = 7.2 Hz, 3 H), 1.47 (s, 9 H), 2.59 (dd, J = 2.4, 14.8 Hz, 1 H), 2.68 (dd, J = 6.4, 16.1 Hz, 1 H), 2.82 (dd, J = 6.6, 16.1 Hz, 1 H), 3.06 (dd, J = 5.1, 14.8 Hz, 1 H), 4.15 (q, J = 7.2, 2 H), 4.24 (m, 1 H), 6.53 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.0, 28.0, 37.6, 39.9, 53.0, 60.8, 82.0, 153.9, 167.4, 170.3; MS (EI) 172 (32), 157 (18), 141 (12), 126 (19), 113 (9), 91 (26), 85 (100); HRMS m/z calcd for $C_{12}H_{20}N_2O_5$ (M^+) 272.1372, found 272.1370.

4-[(Ethoxycarbonyl)methyl]-1-[2-(trimethylsilyl)ethoxycarbonyl]azetidin-2-one (50): 41% yield; amber oil; IR (neat) 3291, 2956, 1788, 1737, 1316, 1250, 1183, 1031, 861, 839 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.04, (s, 9 H), 1.02 (t, J = 8.7 Hz, 2 H), 1.26 (t, J = 7.2 Hz, 3 H), 2.60 (dd, J = 2.3, 14.8 Hz, 1 H), 2.69 (dd, J = 6.5, 16.0 Hz, 1 H), 2.82 (dd, J = 6.4, 16.2 Hz, 1 H), 3.08 (dd, J = 5.4, 14.8 Hz, 1 H), 4.15 (q, J = 7.2 Hz, 2 H), 4.25 (m, 3 H), 6.68 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ −1.7, 14.0, 17.5, 37.4, 39.9, 53.0, 60.8, 64.7, 155.2, 167.4, 170.3; MS (EI) 244 (1), 202 (5), 157 (10), 117 (2), 101 (11), 73 (100); MS (CI) 317 (20), 289 (55), 273 (23), 245 (100), 157 (10); HRMS m/z calcd for $C_{13}H_{24}N_2O_5Si$ (M^+) 316.1455, found 316.1454.

1-[(*tert*-Butoxycarbonyl)amino]-4,4-dimethylazetidin-2-one (56). In a manner similar to that described previously for the preparation of **40**, **21** was irradiated in methanol through a Vycor filter for 2 h to provide **56** as a colorless oil after purification in 85% yield: IR (neat) 3270, 1772, 1735, 1370, 1277, 1247, 1157 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.43 (s, 6 H), 1.50 (s, 9 H), 2.77 (s, 2 H), 6.35 (br s, 1 H); MS (EI) 214 (7), 176 (5), 155 (5), 141 (22), 114 (34), 99 (15), 83 (30), 72 (100); HRMS m/z calcd for $C_{10}H_{18}N_2O_3$ (M^+) 214.1318, found 214.1317.

1-Amino-3-methylazetidin-2-one (57). To a solution of **41**

(25 mg, 0.11 mmol) in 10 mL of ethyl acetate under an atmosphere of hydrogen was added 6 mg of Pd on carbon with vigorous stirring. After 6 h the reaction mixture was filtered through a bed of Celite and rinsed with ethyl acetate. The solution was concentrated in vacuo to an oil. Purification by column chromatography on silica gel with 10% methanol–chloroform as the elutant gave 8 mg (73%) of **57** as a pale yellow oil: IR (neat) 3449, 3332, 2971, 1745, 1457, 1245, 1091 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.27 (d, J = 7.2 Hz, 3 H), 2.92 (m, 1 H), 2.98 (m, 1 H), 3.56 (t, J = 4.9 Hz, 1 H), 4.05 (br s, 2 H); ^{13}C NMR ($CDCl_3$) δ 13.1, 41.2, 53.2, 171.2; MS (EI) 100 (73); MS (CI) 100 (16), 91 (44), 79 (100); HRMS m/z calcd for $C_4H_8N_2O$ (M^+) 100.0637, found 100.0637.

General Procedure for the Preparation of 1-Aminoazetidin-2-ones. As a typical example, cleavage of the (trimethylsilyl)ethoxycarbonyl group of 4-methyl-1-[[2-(trimethylsilyl)ethoxycarbonyl]amino]azetidin-2-one (**42**) was carried out in the following manner. **1-Amino-3-methylazetidin-2-one (57).** To a solution of **42** (111 mg, 0.45 mmol) in 20 mL of acetonitrile was added dropwise 0.47 mL (0.47 mmol) of tetra-*n*-butylammonium fluoride (1.0 M in THF) with stirring. The solution was heated at 50 °C for 3 h under argon. The solution was then cooled to ambient temperature, three drops of water were added, and the solution was concentrated in vacuo to give an oil. Purification by column chromatography on silica gel with 10% methanol–chloroform as the elutant yielded 33 mg (73%) of **57**.

1-Amino-4-methylazetidin-2-one (58): 58% yield; amber oil; IR (neat) 3438, 3329, 1748, 1382, 1204, 1081, 1004 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.33 (d, J = 6.1 Hz, 3 H), 2.32 (dd, J = 2.2, 14.2 Hz, 1 H), 2.89 (dd, J = 5.0, 14.2 Hz, 1 H), 3.68 (m, 1 H), 3.90 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 17.4, 41.2, 52.6, 167.7; MS (EI) 100 (13), 86 (6); HRMS m/z calcd for $C_4H_8N_2O$ (M^+) 100.0637, found 100.0637.

***cis*-1-Amino-3,4-dimethylazetidin-2-one (59):** 73% yield; white solid; mp 80–81 °C (ether); IR (neat) 3324, 3198, 2973, 1746, 1462, 1379, 1350, 1034, 894 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.11 (d, J = 7.6 Hz, 3 H), 1.19 (d, J = 6.3 Hz, 3 H), 3.04 (dq, J = 2.2, 5.3 Hz, 1 H), 3.77 (m, 1 H), 3.84 (br s, 2 H); ^{13}C NMR ($CDCl_3$) δ 8.5, 12.5, 44.1, 56.3, 171.4; MS (EI) 114 (62), 99 (19), 86 (21), 73 (53), 58 (100); HRMS m/z calcd for $C_5H_{10}N_2O$ (M^+) 114.0794, found 114.0794. Anal. Calcd for $C_5H_{10}N_2O$: C, 52.59; H, 8.85; N, 24.54. Found: C, 52.88; H, 8.84; N, 24.82.

***trans*-1-Amino-3,4-dimethylazetidin-2-one (60):** 84% yield; pale yellow oil; IR (neat) 3226, 3201, 2967, 1752, 1454, 1379, 1356, 893 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.23 (d, J = 7.4 Hz, 3 H), 1.30 (d, J = 6.1 Hz, 3 H), 2.51 (dq, J = 1.5, 7.2 Hz, 1 H), 3.30 (dq, J = 1.7, 6.1 Hz, 1 H), 3.62 (br s, 2 H); ^{13}C NMR ($CDCl_3$) δ 12.5, 16.7, 49.2, 61.1, 171.0; MS (EI) 114 (42), 100 (16), 83 (41), 73 (26), 58 (100); HRMS m/z calcd for $C_5H_{10}N_2O$ (M^+) 114.0794, found 114.0794. Anal. Calcd for $C_5H_{10}N_2O$: C, 52.59; H, 8.85; N, 24.54. Found: C, 52.66; H, 8.97; N, 24.32.

1-Aminoazetidin-2-one (61): 88% yield; white solid; mp 92–93.5 °C (ether): IR (film) 3296, 3200, 1731, 1619, 1090, 977 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.76 (t, J = 4.0 Hz, 2 H), 3.41 (t, J = 4.0 Hz, 2 H), 3.98 (br s, 2 H); ^{13}C NMR ($CDCl_3$) δ 33.6, 45.0, 168.1; MS (EI) 86 (100). Anal. Calcd for $C_3H_6N_2O$: C, 41.84; H, 7.04; N, 32.54. Found: C, 41.53; H, 7.05; N, 32.32.

1-Amino-4-[(ethoxycarbonyl)methyl]azetidin-2-one (62): 33% yield; amber oil; IR (neat) 3451, 3340, 2983, 1757, 1732, 1381, 1256, 1184, 1028 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (t, J = 7.1 Hz, 3 H), 2.47 (dd, J = 2.2, 14.3 Hz, 1 H), 2.57 (dd, J = 6.9, 15.8 Hz, 1 H), 2.77 (dd, J = 5.8, 15.9 Hz, 1 H), 2.93 (dd, J = 5.0, 14.6 Hz, 1 H), 3.95 (m, 3 H), 4.14 (q, J = 7.1 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 14.1, 37.1, 39.8, 53.1, 60.9, 167.2, 170.4; MS (EI) 167 (12), 156 (4), 125 (100), 99 (16), 83 (26); MS (CI) 213 (100), 171 (85), 156 (5), 135 (6), 125 (28), 99 (12); HRMS m/z calcd for $C_7H_{12}N_2O_3$ (M^+) 172.0848, found 172.0848. Anal. Calcd for $C_7H_{12}N_2O_3$: C, 49.43; H, 6.70; N, 14.24. Found: C, 48.96; H, 6.59; N, 13.94.

4-(2′-Hydroxyethyl)pyrazolidin-3-one (65). To a solution of **64**[25] (825 mg, 6.42 mmol) in 15 mL of absolute methanol was added hydrazine hydrate (0.34 mL, 1.06 mmol) by syringe. The resulting solution was heated at reflux for 4 h and then concentrated in vacuo to a viscous oil. Purification by column chromatography on silica gel with 15% methanol–chloroform as the elutant provided 634 mg (76%) of a 1:1 mixture of diastereomeric pyrazolidin-3-ones. Compound **65**[24] eluted from the column after its stereoisomer; IR (neat) 3500–3000 (br), 1681 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20 (d, J = 6.5 Hz, 3 H), 2.54 (m, 1 H), 3.48 (s, 1 H), 3.55 (m, 2 H), 4.30 (dq, J = 6.5, 2.5 Hz, 1 H), 5.65 (br s, 2 H); ^{13}C NMR ($CDCl_3$) δ 21.3, 45.9, 49.6, 64.9, 177.3; MS (EI) 130 (20), 112 (29), 85 (100), 69 (50); HRMS m/z calcd for $C_5H_{10}O_2N_2$ (M^+) 130.0742, found 130.0741.

4-[2′-[(*tert*-Butyldimethylsilyl)oxy]ethyl]-1-(*o*-nitrobenzyl)pyrazolidin-3-one (66). *o*-Nitrobenzylation of **65** was carried out in a manner similar to that described for the preparation of **22** originating with **65** (1.57 g 12.1 mmol). Without purification, the crude *o*-nitrobenzylated product (3.50 g) was diluted with 75 mL of dimethylformamide and *tert*-butyldimethylsilyl chloride (2.0 g, 13.3 mmol) was added along with imidazole (1.36 g, 19.9 mmol). The mixture was stirred under argon at room temperature for 24 h and then partitioned between 30 mL of water and 30 mL of ether. The aqueous layer was washed with 2 × 30 mL of ether, and the organic layers were combined, dried with $MgSO_4$, and concentrated in vacuo. Purification by column chromatography on silica gel with 1:1 ethyl acetate–hexane as the elutant afforded 2.59 g (56% based on **65**) of **66** as a yellow solid: mp 138–141 °C; IR (neat) 2955, 2929, 1696, 1528, 836, 668 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.05 (s, 3 H), 0.07 (s, 3 H), 0.87 (s, 9 H), 1.17 (d, J = 6.3 Hz, 3 H), 2.73 (m, 1 H), 3.36 (m, 1 H), 3.53 (m, 1 H), 4.21 (s, 2 H), 4.33 (m, 1 H), 6.67 (s, 1 H), 7.48 (m, 1 H), 7.59 (m, 2 H), 7.67 (d, 1 H); ^{13}C NMR ($CDCl_3$) δ −4.9, −4.6, 17.9, 18.9, 25.7, 47.6, 53.4, 61.1, 66.4, 125.0, 128.9, 130.9, 131.5, 133.2, 149.3, 174.1; MS (CI) 380 (100), 364 (26), 322 (39), 248 (15), 159 (18), 120 (19), 75 (14); HRMS m/z calcd for $C_{18}H_{29}O_4N_3Si$ (M^+) 379.1927, found (M + 1) 380.2006. Anal. Calcd for $C_{18}H_{29}O_4N_3Si$: C, 56.96; H, 7.71; N, 11.08. Found: C, 57.20; H, 7.80; N, 11.13.

2-[2-(Trimethylsilyl)ethoxycarbonyl]-1-(*o*-nitrobenzyl)-4-[2′-[(*tert*-butyldimethylsilyl)oxy]ethyl]-pyrazolidin-3-one (67). The preparation of **67** was carried out in a manner similar to that described for the preparation of **30**: 64% yield; colorless solid; mp 85–88 °C (ether–hexane); IR (neat) 2955, 1788, 1734, 1528, 1347, 1288, 1252, 859, 838, 779 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.03 (s, 3 H), 0.04 (s, 3 H), 0.05 (s, 9 H), 0.80 (s, 9 H), 1.08 (m, 2 H), 1.13 (d, J = 6.5 Hz, 3 H), 2.99 (m, 1 H), 3.14 (dd, J = 11.9, 12.0 Hz, 1 H), 3.62 (t, J = 11.7 Hz, 1 H), 4.34 (m, 5 H), 7.47 (m, 1 H), 7.65 (m, 1 H), 7.94 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ −5.2, −4.5, −1.6, 17.6, 17.8, 22.3, 25.7, 48.0, 56.9, 65.6, 65.7, 124.5, 128.6, 131.4, 131.9, 133.3, 149.9, 172.0; MS (CI) 524 (13), 496 (100), 480 (57), 452 (56), 73 (38), 41 (49); HRMS m/z calcd for $C_{24}H_{41}O_6N_3Si_2$ (M^+) 523.2534, found (M + 1) 524.2612.

3-[2′-[(*tert*-Butyldimethylsilyl)oxy]ethyl]-1-[[(trimethylsilyl)ethoxycarbonyl]amino]azetidin-2-one (68). This compound was prepared in a manner similar to that described for the preparation of **40**: 60% yield; colorless oil; IR (neat) 3275, 2955, 2930, 1786, 1733, 1515, 1472, 1179, 1062, 1046, 836 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.04 (s, 9 H), 0.06 (s, 3 H), 0.07 (s, 3 H), 0.86 (s, 9 H), 0.99 (m, 2 H), 1.23 (d, J = 6.1 Hz, 3 H), 3.08 (m, 1 H), 3.51 (m, 1 H), 3.62 (m, 1 H), 4.22 (m, 3 H), 6.66 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ −5.0, −4.3, −1.6, 17.7, 17.9, 22.8, 25.6, 47.3, 55.3, 64.9, 65.7, 154.9, 168.8; MS (CI) 389 (17), 361 (78), 345 (100), 331 (22), 317 (69), 185 (26), 73 (66); HRMS m/z calcd for $C_{17}H_{36}O_4N_2Si_2$ (M^+) 388.2214, found (M + 1) 389.2292.

1-Amino-3-[2′-[(*tert*-butyldimethylsilyl)oxy]ethyl]azetidin-2-one (69). This compound was prepared in a manner similar to that described for the preparation of **57**: 65% yield; colorless oil: IR (neat) 3332 (br), 2959, 2932, 2858, 1760, 1468, 1369, 1137, 1106, 1078, 1018, 985, 838, 778 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.06 (s, 6 H), 0.86 (s, 9 H), 1.18 (d, J = 6.2 Hz, 3 H), 2.97 (m, 1 H), 3.39 (m, 1 H), 3.46 (m, 1 H), 3.96 (s, 2 H), 4.16 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ −5.05, −4.24, 17.9, 22.8, 25.7, 47.3, 54.6, 65.0, 168.7; MS (CI) 245 (51), 229 (69), 187 (85), 83 (30), 49 (40); HRMS m/z calcd for $C_{11}H_{24}O_2N_2$ (M^+) 244.1607, found 245.1685 (M + 1). Anal. Calcd for $C_{11}H_{24}O_2N_2Si$: C, 54.06; H, 9.91; N, 11.47. Found: C, 53.89; H, 10.02; N, 11.26.

1-Amino-3-(2′-hydroxyethyl)azetidin-2-one (70). This compound was obtained upon further exposure of **69** to tetra-*n*-butylammonium fluoride as described for the preparation of **57**: colorless oil; IR (neat) 3329–3205 (br), 2969, 1744, 1138, 1091, 1011, 795 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.27 (d, J = 6.5 Hz, 3 H), 2.22 (br s, 1 H), 3.05 (m, 1 H), 3.46 (m, 2 H), 4.07 (br s, 2 H), 4.19 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 21.7, 47.7, 54.0, 64.8, 168.7; MS (EI) 130 (5), 112 (25), 85 (36), 69 (98), 55 (100), 45 (79); HRMS m/z calcd

for $C_5H_{10}O_2N_2$ (M^+) 130.0742, found 130.0741.

Acknowledgment. We are grateful to Alan T. Johnson for the X-ray structure determination of the cis isomer of compound **36**. Financial support was provided by the National Science Foundation (CHE-8619029). Funds for the purchase of a Bruker AC-300 MHz NMR spectrometer were provided by the National Science Foundation (1 S10 RR 04039-01).

Supplementary Material Available: Tables listing the crystallographic data collection details, refinement procedures, bond lengths, bond angles, positional parameters, and thermal parameters of *cis*-4,5-dimethyl-1-(*o*-nitrobenzyl)-2-[2-(trimethylsilyl)ethoxycarbonyl]pyrazolidin-3-one, **36** (13 pages). Ordering information is given on on any current masthead page.

Notes

Polymer-Supported Poly(amino acids) as New Asymmetric Epoxidation Catalyst of α,β-Unsaturated Ketones

Shinichi Itsuno,* Minako Sakakura, and Koichi Ito

Department of Materials Science, Toyohashi University of Technology, Tempaku-cho, Toyohashi, 440 Japan

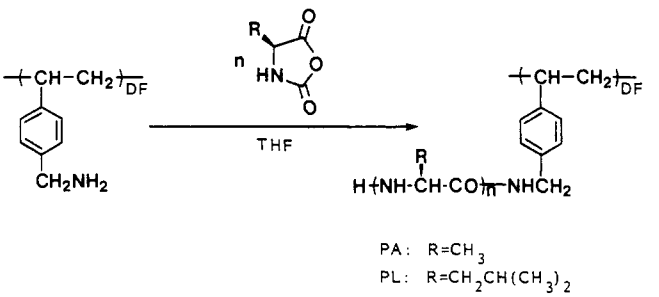
Received April 23, 1990

Recently there has been much work on polymer-supported asymmetric syntheses.[1] The polymers, in insoluble beads form, offer a well-documented advantage in purification since separation of chiral reaction product from the chiral auxiliary is achieved by filtration.[2] The polymers can be recycled and may provide a unique microenvironment that may result in enhanced stereoselectivities.

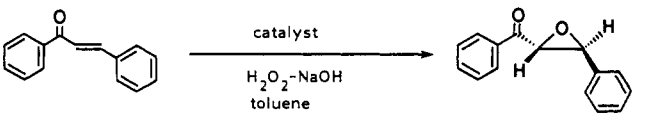
Asymmetric reactions in which peptides or poly(amino acids) take part include Michael additions of active hydrogen compounds to activated double bonds,[3] carbonylation of allylic alcohols,[4] hydrogenation,[5] oxidation,[6] and reduction.[7] Among the most interesting asymmetric syntheses using poly(amino acids) are the epoxidations of α,β-unsaturated carbonyl compounds reported by Juliá and his group.[8] Enantioselectivities higher than 90% with poly(L-alanine) as chiral catalyst have been reported. A considerable drawback to this system is the difficulty of separation and recycling of the semisolid pastelike poly(amino acid).

We have found that poly(styrene-co-divinylbenzene)-supported poly(amino acid) can act as an efficient chiral catalyst in the epoxidation of α,β-unsaturated carbonyl compounds with alkaline hydrogen peroxide to yield optically active epoxy ketones in high enantioselectivities up to 99%. Separation of the polymer-supported catalyst has been remarkably improved in this system, and they could be reused without a significant loss of activity as will be discussed in this paper.

Scheme I



Scheme II



Polymer-supported poly(amino acids) were synthesized by the following procedure. A 2% cross-linked microporous polystyrene resin incorporating aminomethyl functionality was prepared as a starting material. Utilizing this polymeric primary amine as an initiator, *N*-carboxyanhydrides (NCA) of L-alanine and L-leucine were polymerized in THF at room temperature for 40 h under a nitrogen atmosphere to obtain the polymer-supported poly(L-alanine) (PA) and poly(L-leucine) (PL), respectively, with different degrees of polymerization (n), depending upon the NCA:initiator ratio (Scheme I). The aminomethyl group of highly cross-linked macroporous polystyrene containing 20 mol % of divinylbenzene was not suited for this grafting reaction since the resin has no swellability in organic solvents (ML). We have also prepared linear polystyrene-based catalyst (LL).

The various polymer-supported poly(amino acids) (PA1-PA8, PL1-PL6, ML, and LL) were tested as chiral catalysts in the epoxidation of benzalacetophenone according to Juliá's procedure.[8] The reactions were carried out at room temperature in a triphase system with toluene, water, polymeric catalyst, and oxidant (H_2O_2–NaOH), unless otherwise stated (Scheme II). The results are summarized in Table I. Satisfactory enantioselectivities were obtained by using both PA and PL as asymmetric

(1) (a) Itsuno, S.; Sakurai, Y.; Ito, K.; Maruyama, T.; Nakahama, S.; Fréchet, J. M. *J. Org. Chem.* **1990**, *55*, 304. (b) Hodge, P. *Syntheses and Separations Using Functional Polymers*; Sherrington, D. C., Hodge, P., Eds.; Wiley: Chichester, 1988; p 43. (c) Blossey, E. C.; Ford, W. T. *Comprehensive Polymer Science*; Allen, G., Ed.; Pergamon Press: Oxford, 1989; Vol. 6, p81.

(2) Merrifield, R. B. *J. Am. Chem. Soc.* **1963**, *85*, 2149. *Polymer Supported Reaction in Organic Synthesis*; Hodge, P., Sherrington, D. C., Eds.; Wiley: New York, 1980.

(3) Inoue, S. *Adv. Polym. Sci.* **1976**, *21*, 78. Ueyanagi, K.; Inoue, S. *Makromol. Chem.* **1977**, *178*, 235.

(4) Alper, H.; Hamel, N. *J. Chem. Soc., Chem. Commun.* **1990**, 135.

(5) Beamer, R. L.; Belding, R. H.; Fickling, C. S. *J. Pharm. Sci.* **1969**, *58*, 1419.

(6) Sugimoto, T.; Matsumura, Y.; Tanimoto, S.; Okano, M. *J. Chem. Soc., Chem. Commun.* **1978**, 926.

(7) Baba, N.; Matsumura, Y.; Sugimoto, T. *Tetrahedron Lett.* **1978**, 4281.

(8) (a) Juliá, S.; Masana, J.; Vega, J. C. *Angew. Chem., Int. Ed. Engl.* **1980**, 929. (b) Juliá, S.; Guixer, J.; Masana, J.; Rocas, J.; Colonna, S.; Annuziata, R.; Molinari, H. *J. Chem. Soc., Perkin Trans 1* **1982**, 1317. (c) Colonna, S.; Molinari, H.; Banfi, S.; Juliá, S.; Masana, J.; Alvarez, A. *Tetrahedron* **1983**, *39*, 1635. (d) Banfi, S.; Colonna, S.; Molinari, H.; Juliá, S.; Guixer J. *Tetrahedron* **1984**, *40*, 5207.

0022-3263/90/1955-6047$02.50/0