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Synthesis and Photolysis of 2-Acylpyrazolidin-3-ones. A Model for the Photochemical Syntheses of 6-Azapenicillin Isomers[1]

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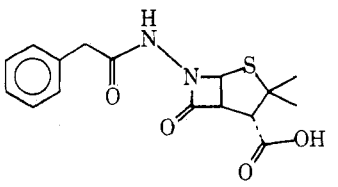
A series of 2-acyl-5,5-dimethylpyrazolidin-3-ones (**5a–e**) was prepared by two routes and shown to rearrange photochemically under a variety of conditions to *N*-acylamino-4,4-dimethylazetidin-2-ones (**9a–e**). Photolysis of the parent systems, 5,5-dimethylpyrazolidin-3-one (1), to give 1-amino-4,4-dimethylazetidin-2-one (**20**), which was acylated to give **9a**, is also discussed. A plausible reaction scheme is presented to account for the observed photochemistry.

Strong interest in the synthesis of β-lactam (azetidin-2-one) containing molecules,[2] particularly those of the penicillin and cephalosporin classes of antibiotics,[3] has continued unabated since the original discovery and structure determination of penicillin.[4] Although a large number of original syntheses of β-lactams have been reported since that period, very few of these approaches have employed either thermal[5] or photochemical[6] ring contraction steps. As a part of our approach to the synthesis of penicillin isomers containing nitrogen in the 6 position (such as I), we hope to use a photochemically induced ring contraction reaction to generate the β-lactam moiety. As a model system for such a step we have investigated the photochemistry of a series of 2-acyl-5,5-dimethylpyrazolidin-3-ones, one of which contains the side chain of penicillin G.[7] We report at this time some interesting aspects of the syntheses of these 2-acylpyrazolidin-3-ones[8] and our studies on their photochemical rearrangements to give *N*-acylamino β-lactams.



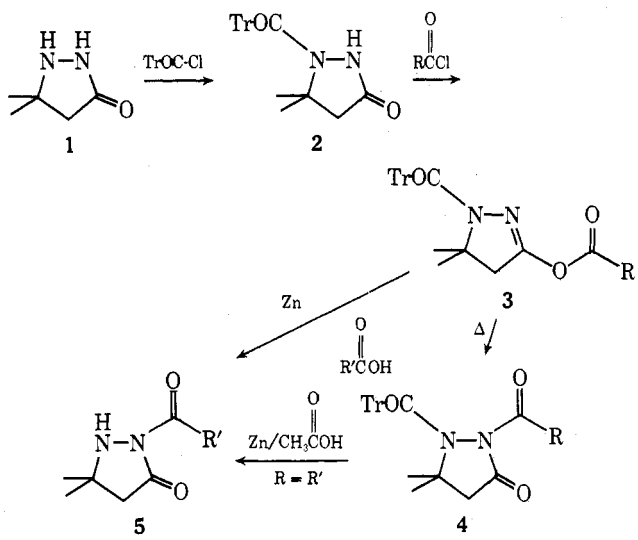
I

Preparation of 2-Acyl-5,5-dimethylpyrazolidin-3-ones. After several attempts to condense acylhydrazides with 3,3-dimethylacrylic acid[9] or its ethyl ester resulted only in the isolation of 1,2-diacylhydrazides, a different approach involving functionalization of the preformed ring

system, 5,5-dimethylpyrazolidin-3-one (1), was undertaken. While 1-acyl derivatives of 5,5-dimethylpyrazolidin-3-ones can be prepared easily, our attempts to form 2-acyl isomers by reaction of the anion of 1, generated in situ, with a variety of electrophilic species led only to complex mixtures containing no isolatable products with the properties expected for the 2-acylpyrazolidin-3-ones. When the amine nitrogen of 1 was protected using a removable acyl blocking group, however, the desired 2-acyl isomers were obtained in good yields.

The protected ring system, 1-(2,2,2-trichloroethoxycarbonyl[10])-5,5-dimethylpyrazolidin-3-one (2, Scheme I)

Scheme I



a, R = CH_3; b, R = CH_2CH_3; c, R = $CH(CH_3)_2$; d, R = $C(CH_3)_3$; e, R = CH_2Ph; f, R = Ph

a, R′ = CH_3; b, R′ = CH_2CH_3; c, R′ = $CH(CH_3)_2$; d, R′ = $C(CH_3)_3$

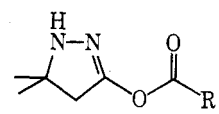
TrOC = Cl_3CCH_2OC(=O)-

was prepared from 1[11] using Schotten–Baumann conditions. Reaction of 2 with 1 equiv of acetyl chloride and triethylamine in tetrahydrofuran solvent at room temperature gave exclusively **3a**, the *O*-acetyl derivative of **2**. Heating of **3a** neat for 3 hr at 110° resulted in a high yield of **4a**, the *N*-acetyl isomer of **3a**. This thermal rearrangement could be followed very easily, since the *O*-acetyl (**3a**) and *N*-acetyl (**4a**) derivatives of 2 were readily distinguished by their NMR spectra. The NMR spectrum of the *O*-acetyl derivative showed a singlet due to the ring methylene protons at δ 3.10 while the *N*-acetyl derivative showed a singlet for these protons at δ 2.70. Consequently, integration of the δ 2.5–3.5 region gave the relative ratio of the two isomers.

When compounds **4b–e** were prepared from **2** using reaction conditions similar to those used to prepare **4a** from **2**, two deviations were noted: first, heating at 110° for 3 hr of **3d**, which contains a bulky *tert*-butyl group, resulted in a mixture of **3d** and **4d** of which **4d**, the *N*-acyl derivative of **2**, comprised only about 40% as determined by NMR (in our hands further heating did not alter the above ratio); second, acylation of **2** with phenylacetyl chloride gave an appreciable amount of **4e**, the *N*-acyl derivative of **2**, along with the expected *O*-acyl derivative **3e**. Since no *N*-acyl derivatives of **2** were obtained during the similar acylations of **2** to give **3a–d**, we postulate that O-acylation of **2** occurred to give **3e** which subsequently partially isomerized to **4e** under the reaction conditions. The more facile isomerization of **3e**, relative to **3a–d**, is reasonable because the electron-withdrawing inductive effect of the phenyl group makes the side-chain carbonyl more reactive to nucleophilic attack.

It appears that acylation using the conditions described gives the less stable *O*-acyl derivatives of **2**, namely **3**, and the heating of **3** results in equilibration[12] of it with the *N*-acyl derivatives **4**. The position of the equilibrium appears to be influenced by several factors, including the nature of the 1 substituent[13] and steric and electronic factors relating to the added acyl group. The thermal equilibration of the *O*-acyl and *N*-acyl derivatives of this system possibly occurs through a stepwise biomolecular transacylation process.[16]

When the TrOC protecting group was removed from the *N*-acyl derivatives of **2** (**4a–e**) using zinc dust in acetic acid at room temperature, good yields of the desired 2-acyl-5,5-dimethylpyrazolidin-3-ones (**5a–e**), 2-acyl derivatives of **1**, were obtained. As part of the structure proof of compounds **5a–e**, attempts were made to isolate **6a**, the *O*-acetyl derivative of **1**, by careful removal of the protecting group from **3a**. In all cases, however, we obtained only **5a**, the 2-acetyl derivative of **1**. In hopes of obtaining a stable *O*-acyl derivative of **1**, compound **3f**, the *O*-benzoyl derivative of **2**, was prepared. Interestingly, removal of the protecting group from **3f** using zinc in acetic acid at room temperature did not give **6f**, the desired *O*-benzoyl derivative of **1**, or its 2-benzoyl isomer **5f**, but instead gave a good yield of the 2-acetyl derivative **5a** where the acetyl moiety appears to have been derived from the carboxylic acid solvent (acetic acid). This interesting "exchange–rearrangement" reaction of **6f** also occurred when either propionic acid, isobutyric acid, or a mixture of pivalic acid and tetrahydrofuran (50:50 by volume) was used as the solvent, giving respectively **5b–d**. Several attempts to obtain **6f** from **3f** by removal of the protecting group under conditions not involving a carboxylic acid solvent were unsuccessful.



6a, R = CH_3; f, R = Ph

Formation of **5a** upon treatment of **3f** with zinc in acetic acid seems to involve two steps: one, loss of the protecting group; and two, acyl exchange–rearrangement. It appears that loss of the protecting group must occur before the exchange–rearrangement reaction, since treatment of **3f**, the *O*-benzoyl derivative of **2**, with either acetic acid or acetic acid containing zinc acetate resulted only in the slow formation of **2**. No *O*-acetyl (**3a**), *N*-acetyl (**4a**), or *N*-benzoyl (**4f**) derivatives of **2** could be isolated in the absence of metallic zinc. A mechanism[17] consistent with our observations for the conversion of **3f** to **5a** is shown in Scheme II. We postulate that **6f** is an intermediate in the reaction and that **6f** reacts with the solvent to form species **7** which breaks down as shown to give the observed products. Protonation of the imidic nitrogen of **7** instead of intramolecular transacylation would give **2**, which was detected as a minor product in these acyl exchange–rearrangement reactions. Our failure to isolate either **6a**, the *O*-acetyl derivative of **1**, or **6f**, the *O*-benzoyl derivative of **1**, is not surprising in light of our inability to prepare a 1-benzyl *O*-acyl derivative of this system.[13] The stabilization provided by a 1-acyl substituent is apparently necessary for the isolation under normal conditions of any *O*-acyl derivatives of pyrazolidin-3-ones.

Irradiation of 2-Acyl-5,5-dimethylpyrazolidin-3-ones. Photolysis of 2-acyl-5,5-dimethylpyrazolidin-3-ones

Scheme II

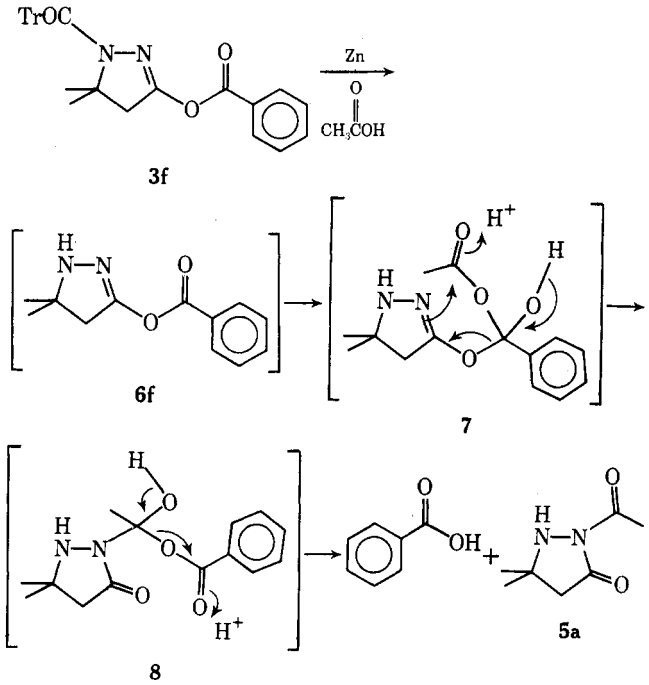
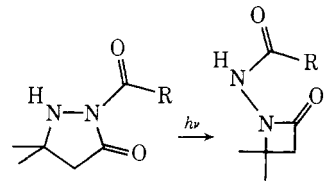


Table I[a]

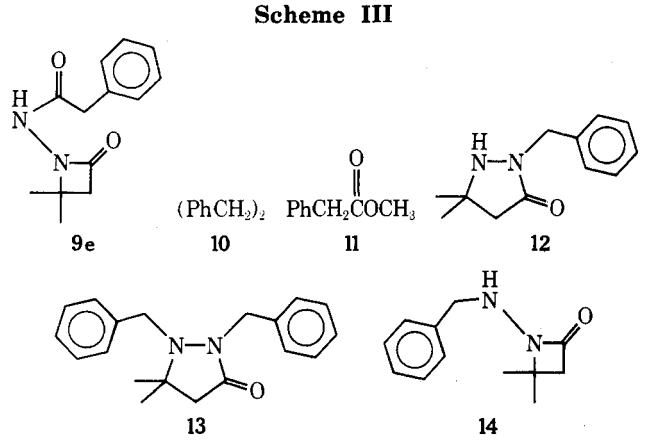


Compd		R	Solvent[b]	Filter	Yield, %[c]
5a	9a	CH_3	CH_3OH	Vycor	65
5b	9b	CH_2CH_3	CH_3OH	Vycor	36
5c	9c	$CH(CH_3)_2$	CH_3OH	Vycor	30
5d	9d	$C(CH_3)_3$	CH_3OH	Vycor	20
5e	9e	CH_2Ph	$(CH_3)_3COH$ (non-degassed)	Corex	45

[a] All irradiations were carried out at 0.1–1% w/v concentration for 2 to 3 hr with a Hanovia 450-W immersion lamp. [b] All solutions were degassed with a stream of nitrogen for 2 hr unless noted. [c] Yield of 9 which was isolated by column chromatography on silicic acid.

5a–e led to 1-acylamino-4,4-dimethylazetidin-2-ones[18] **9a–e** in yields ranging from 20 to 65%, depending on the starting material and conditions as shown in Table I. In all the photolyses reported here loss of starting material was followed by TLC using silicic acid plates. In the acetyl (**5a**) and propionyl (**5b**) cases TLC analysis indicated the formation of one new product with a slightly smaller R_f value than that of starting material. For **5c–e,** however, the TLC plates of the crude reaction mixtures were badly streaked and irradiation times for these molecules were arbitrarily set at 2 hr on the basis of the **5a** and the **5b** photolysis results. Irradiation of compounds **5a–d** gave β-lactams **9a–d** as the only isolated products, while irradiation of compound **5e** gave the series of products shown in Scheme III

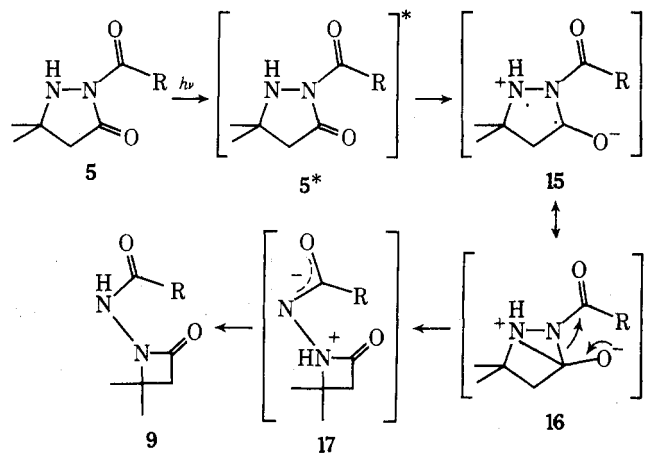
Scheme III



which included **9e.** The yields of the various products were highly condition dependent.[7] It is interesting to note that for the nonaromatic series **5a–d** the pyrazolidin-3-ones show significant uv absorption while the respective azetidin-2-ones show only end absorption. This accounts for the photostability of **9a** when irradiated in methanol through a Vycor filter. In contrast to **9a, 9e** has a uv absorption similar to that of benzene. Irradiation of **9e** in methanol through a Vycor filter for 2 hr led to 15–20% decomposition of the β-lactam.

In order to explain the photochemical ring contraction of **5** to give **9,** the sequence shown in Scheme IV is proposed.

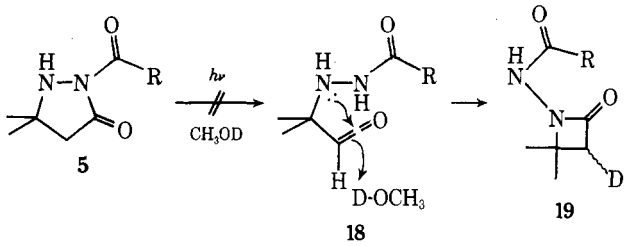
Scheme IV



Formation of radical anion–radical cation species **15** via intramolecular electron transfer deactivation of **5*** followed by bond formation would give **16.**[19] Bond reorganization to give **17** followed by proton transfer would lead to photoproduct **9.** The decrease in the yield of β-lactam in the series **5a–d** (see Table I) can be accounted for by the presence of a photochemical Norrish type I reaction pathway which competes with β-lactam formation. The increasing stability of the radicals formed from type I processes as the substitution of the 2-acyl moiety increases and the decreasing rate of recombination of those radicals once formed can explain the lowered observed yield of β-lactam. Similarily, formation of β-lactam **9e** from **5e** is in competition with type I processes. With **5e,** however, the type I processes are significantly enhanced, giving rise to **10, 12, 13,** and **14** as a result of phenyl-assisted cleavage of the same bond to give stable benzyl radicals. The difference between the yield of **9e** from the photolysis of **5e** in degassed methanol through a Vycor filter (15% of **9e**) and the yield of **9e** from the photolysis of **5e** in nondegassed *tert*-butyl alcohol through a Corex filter (45% of **9e**) probably resulted from quenching of the radical (i.e., type I) processes in the latter case.[20]

In addition to the sequence proposed in Scheme IV, formation of **9** from **5** might be postulated to occur via formation, probably by a Norrish type II process, of a ketene in-

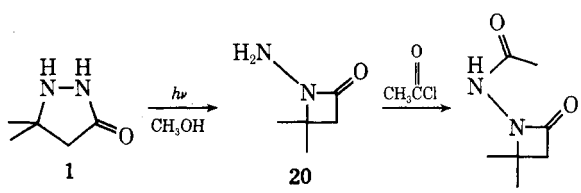
termediate such as **18** followed by closure to the four-membered ring compound **19**.[22] This possibility was ruled out



5 18 19

by photolysis of **5a** in MeOD. Under these conditions the β-lactam product (**19**) would be expected to contain a deuterium in the 3 position. The β-lactam isolated from this photolysis, under conditions which would not cause loss of deuterium from the 3 position, contained no deuterium as determined by mass spectral analysis.

In order to compare the photochemistry of the 2-acylpyrazolidin-3-ones with other derivatives of this ring system, photolysis of the unsubstituted parent compound **1** was undertaken. Irradiation of a degassed methanolic solution of **1** through a Vycor filter for 20 hr, followed by column chromatography of the oil obtained upon evaporation of the solvent, led to a 15% isolated yield of 1-amino-4,4-dimethylazetidin-2-one (**20**).[23] As an internal check **20** was acetylated to give **9a** in good yield. The low yield and long reac-



1 20 9a

tion time required for the formation of **20** from **1** supports the proposed sequence (see Scheme IV) for the formation of β-lactams **9** from the 2-acylpyrazolidin-3-ones **5**. From examination of Scheme IV it can be determined that the presence of a functional group (i.e., an acyl moiety) at the 2 position which can stabilize a negative charge (as in **17**) should strongly enhance β-lactam formation relative to the parent system or a 2-alkyl[15] system. This is, in fact, what is observed.

Further work to expand our understanding of the photochemistry of pyrazolidin-3-ones and the application of these results to the syntheses of penicillin-like bicyclic systems is under way, and will be reported at a later date.

Experimental Section

Melting points were taken in capillary tubes on a Thomas-Hoover Unimelt and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 457 A spectrometer. The NMR spectra were taken either on a Varian A-60 spectrometer or on a Perkin-Elmer Jeol MH-100 spectrometer and are reported in parts per million downfield from tetramethylsilane. Mass spectra were determined on a Perkin-Elmer Hitachi RMU-6D spectrometer. Ultraviolet spectra were taken on a Cary 14 recording spectrophotometer. Gas chromatography was carried out using programmed temperature control on a Hewlett-Packard 5750 B instrument equipped with 8-ft and 10-ft stainless steel columns packed with SE-30 on 80–100 mesh Chromosorb P. Mallinckrodt AR 100 mesh silicic acid was used for all column chromatography. Microanalyses were performed by Galbraith Laboratories, Knoxville, Tenn.

5,5-Dimethylpyrazolidin-3-one (1). Cyclic hydrazide **1** was prepared in 75% yield and has been described previously.[11] For **1**: bp 100° (0.5 mm) [lit.[11] bp 115° (2 mm)]; mass spectrum (70 eV) *m/e* (rel intensity) 114 (21, M^+), 99 (48), 83 (26), 72 (27), 58 (22), 57 (16), 56 (44), 55 (38), 42 (96), 41 (100); uv (EtOH) 202 nm (ε 3750), shoulder 220 (2200).

1-(2,2,2-Trichloroethoxycarbonyl)-5,5-dimethylpyrazolidin-3-one (2). To a solution of 5,5-dimethylpyrazolidin-3-one (**1**, 23.0 g, 0.20 mol) in aqueous 2 *N* NaOH (100 ml) cooled to 10–20° under a nitrogen atmosphere was added dropwise 2,2,2-trichloroethoxycarbonyl chloride (42.5 g, 0.20 mol). After the addition was complete, the mixture was allowed to warm to room temperature and was stirred for 2 hr. The precipitate which formed during the reaction was filtered off and washed with water and a little cold Et_2O. Recrystallization of the solid from EtOH gave 30.2 g (52%) of pure **2**: mp 212.0–212.5°; ir (CCl_3H) 3680, 3400, 1710, 1600, 1372, 1332, 1282, 1120, 1105 cm^{-1}; NMR (CCl_3D) δ 1.65 (s, 6), 2.72 (s, 2), 4.88 (s, 2); mass spectrum (70 eV) *m/e* (rel intensity) 288 [10, isotope ratio shows three chlorines (3-Cl), M^+], 273 (4, 3-Cl), 253 (2, 2-Cl), 141 (20), 131 (30, 3-Cl), 113 (57), 99 (38), 98 (16), 97 (16), 96 (23), 95 (24), 83 (100), 82 (18), 71 (31), 63 (15), 61 (45), 56 (41), 55 (60), 44 (40), 41 (66).

Anal. Calcd for $C_8H_{11}N_2O_3Cl_3$: C, 33.19; H, 3.83; N, 9.68. Found: C, 33.34; H, 3.89; N, 9.74.

2-Acetyl-1-(2,2,2-trichloroethoxycarbonyl)-5,5-dimethylpyrazolidin-3-one (4a) via 3-Acetoxy-1-(2,2,2-trichloroethoxycarbonyl)-5-5-dimethyl-2-pyrazoline (3a). To a solution of 1-(2,2,2-trichloroethoxycarbonyl)-5,5-dimethylpyrazolidin-3-one (**2**, 25.0 g, 0.087 mol) and triethylamine (8.8 g, 0.087 mol) in tetrahydrofuran (475 ml) at room temperature under a nitrogen atmosphere was added dropwise over a period of 30 min acetyl chloride (6.9 g, 0.087 mol). The mixture was stirred for an additional 6 hr and the precipitated triethylamine hydrochloride salt was filtered off. Concentration of the filtrate left a solid which was dried under high vacuum. NMR analysis revealed this to be the O-acylated product **3a**: nmr (CCl_3D) δ 1.68 (s, 6), 2.22 (s, 3), 3.10 (s, 2), 4.89 (s, 2).

Without further purification the O-acylated material was heated neat under a nitrogen atmosphere at 110° for 3 hr. To the solid obtained on cooling was added Et_2O (50–100 ml). A small amount of insoluble material was filtered off and recrystallized from EtOH. Spectral comparisons showed it to be **2**. The Et_2O was stripped to leave a solid which upon recrystallization from Et_2O gave 19.5 g (67% based on **2**) of pure **4a**: mp 83.5–84.5°; ir (CCl_4) 2960, 1750 (broad), 1375, 1340, 1290, 1245, 1210, 1160, 1125, 1105, 1060 cm^{-1}; NMR (CCl_3D) δ 1.60 (s, 6), 2.58 (s, 3), 2.72 (s, 2), 4.82 (s, 2); mass spectrum (70 eV) *m/e* (rel intensity) 330 (trace, 3-Cl, M^+), 288 (45, 3-Cl), 273 (24, 3-Cl), 253 (6, 2-Cl), 183 (8), 141 (11), 131 (15, 3-Cl), 113 (37), 99 (62), 97 (10), 95 (14), 83 (63), 82 (12), 71 (9), 61 (8), 56 (31), 55 (22), 43 (100), 41 (21).

Anal. Calcd for $C_{10}H_{13}N_2O_4Cl_3$: C, 36.22; H, 3.95; N, 8.45. Found: C, 36.16; H, 3.89; N, 8.57.

1-(2,2,2-Trichloroethoxycarbonyl)-5,5-dimethyl-2-propionylpyrazolidin-3-one (4b) via 1-(2,2,2-Trichloroethoxycarbonyl)-5,5-dimethyl-3-propionoxy-2-pyrazoline (3b). Pyrazoline **3b** was prepared in a manner similar to that described for the preparation of **3a**. For **3b**: NMR (CCl_3D) 1.20 (t, J = 7 Hz, 3), 1.68 (s, 6), 2.53 (q, J = 7 Hz), 3.10 (s, 2), 4.89 (s, 2).

Heating of **3b** (110° for 3 hr) followed by recrystallization of the crude product from Et_2O resulted in 53% yield (based on **2**) of pure **4b**: mp 53.0–54.5°; ir (CCl_4) 2970, 1745 (broad), 1385, 1235, 1205, 1130, 1105, 1055 cm^{-1}; NMR (CCl_3D) δ 1.20 (t, J = 7 Hz, 3), 1.60 (s, 6), 2.73 (s, 2), 2.94 (q, J = 7 Hz, 2), 4.81 (s, 2); mass spectrum (70 eV) *m/e* (rel intensity) 344 (1, 3-Cl, M^+) 288 (49, 3-Cl), 273 (21, 3-Cl), 253 (5, 2-Cl), 197 (5), 155 (4), 149 (6), 141 (6), 131 (13, 3-Cl), 113 (25), 99 (40), 97 (10), 95 (13), 83 (42), 71 (8), 61 (9), 57 (100), 56 (38), 55 (19), 43 (10), 42 (10), 41 (22).

Anal. Calcd for $C_{11}H_{15}N_2O_4Cl_3$: C, 38.24; H, 4.38; N, 8.11. Found: C, 38.54; H, 4.51; N, 8.39.

1-(2,2,2-Trichloroethoxycarbonyl)-2-isobutyryl-5,5-dimethylpyrazolidin-3-one (4c) via 1-(2,2,2-Trichloroethoxycarbonyl)-3-isobutyroxy-5,5-dimethyl-2-pyrazoline (3c). Pyrazoline **3c** was prepared in a manner similar to that described for the preparation of **3a**. For **3c**: NMR (CCl_3D) δ 1.28 (d, J = 7 Hz, 6), 1.68 (s, 6), 3.12 (s, 2), 3.25 (septet, J = 7 Hz, 1), 4.90 (s, 2).

Heating of **3c** (110° for 3 hr) followed by recrystallization of the crude product from Et_2O resulted in a 48% yield (based on **2**) of pure **4c**: mp 81–82°; ir (CCl_4) 2970, 1740 (shoulder 1760), 1390, 1235, 1200, 1130, 1105, 1050 cm^{-1}; NMR (CCl_3D) δ 1.24 (d, J = 7 Hz, 6), 1.59 (s, 6), 2.25 (s, 2), 3.65 (septet, J = 7 Hz, 1), 4.82 (s, 2); mass spectrum (70 eV) *m/e* (rel intensity) 358 (trace, 3-Cl, M^+), 288 (19, 3-Cl), 273 (7.5, 3-Cl), 253 (2, 2-Cl), 211 (2.5), 169 (1.5), 149 (2), 141 (4.5), 131 (8, 3-Cl), 113 (13), 99 (22), 97 (6), 95 (8), 83 (23), 82 (4), 71 (61), 61 (5), 56 (18), 55 (12), 43 (100), 41 (33).

Anal. Calcd for $C_{12}H_{17}N_2O_4Cl_3$: C, 40.08; H, 4.77; N, 7.79. Found: C, 40.03; H, 4.70; N, 7.80.

1-(2,2,2-Trichloroethoxycarbonyl)-5,5-dimethyl-2-pivaloylpyrazolidin-3-one (4d) via 1-(2,2,2-Trichloroethoxycarbonyl)-

5,5-dimethyl-3-pivaloxy-2-pyrazoline (3d). Pyrazoline **3d** was prepared in a manner similar to that described for the preparation of **3a.** For **3d:** NMR (CCl_3D) δ 1.31 (s, 9), 1.78 (s, 6), 3.09 (s, 2), 4.89 (s, 2).

Heating of **3d** (120° for 10 hr) resulted in partial conversion (40% as determined by the appearance of new signals in the NMR) to **4d:** NMR (CCl_3D) δ 1.39 (s, 9), 1.60 (s, 6), 2.72 (s, 2), 4.79 (s, 2).

1-(2,2,2-Trichloroethoxycarbonyl)-5,5-dimethyl-2-phenylacetylpyrazolidin-3-one (4e) via 1-(2,2,2-Trichloroethoxycarbonyl)-5,5-dimethyl-3-phenylacetoxy-2-pyrazoline (3e). Treatment of **2** with phenylacetyl chloride, under conditions similar to those used for the preparation of **3a,** gave a 30:60 mixture of **3e** and **4e.** The signals assigned to **3e** follow: NMR (CCl_3D) δ 1.59 (s, 6), 3.00 (s, 2), 3.72 (s, 2), 4.82 (s, 2), 7.26 (s, 5).

Heating of the mixture (110° for 3 hr) followed by recrystallization of the crude product from Et_2O resulted in a 60% yield (based on **2**) of pure **4e:** mp 74–75°; ir (CCl_4) 2960, 1750 (broad), 1450, 1410, 1390, 1380, 1340, 1225, 1205, 1125, 1095, 1055 cm^{-1}; NMR (CCl_3D) δ 1.52 (s, 6), 2.65 (s, 2), 4.28 (s, 2), 4.75 (s, 2), 7.29 (s, 5); mass spectrum (70 eV) *m/e* (rel intensity) no parent ion, 308 (2), 288 (5, 3-Cl), 273 (3, 3-Cl), 253 (1), 204 (2), 203 (3), 159 (2), 141 (8), 136 (24), 131 (12, 3-Cl), 119 (25), 105 (40), 99 (19), 97 (11), 92 (23), 91 (100), 83 (43), 77 (11), 71 (12), 65 (18), 63 (11), 61 (19), 56 (26), 55 (28), 44 (56), 41 (44).

Anal. Calcd for $C_{16}H_{17}N_2O_4Cl_3$: C, 47.14; H, 4.20; N, 6.87. Found: C, 47.31; H, 4.18; N, 6.96.

3-Benzoxy-1-(2,2,2-trichloroethoxycarbonyl)-5,5-dimethyl-2-pyrazoline (3f). Pyrazoline **3f** was prepared in 70% yield in a manner similar to that described for the preparation of **3a.** For **3f:** mp 124–125° ir (CCl_4) 3050, 2960 (shoulder 2940), 1755, 1720, 1425, 1325, 1250 (shoulder 1240), 1210, 1175, 1110, 1075, 1055, 1020, 960 cm^{-1}; NMR (CCl_3D) δ 1.72 (s, 6), 3.28 (s, 2), 4.91 (s, 2), 7.50–7.80 (m, 3), 8.05–8.30 (m, 2); mass spectrum (70 eV) *m/e* (rel intensity) 392 (1, 3-Cl, M^+), 357 (0.5, 2-Cl), 288 (0.5, 3-Cl) 273 (trace, 3-Cl), 245 (1.5), 266 (trace), 218 (trace), 307 (0.7), 198 (trace), 159 (trace), 141 (0.8), 133 (1), 131 (1), 122 (2.5), 113 (1.5) 106 (8), 105 (100), 99 (0.5), 97 (1), 95 (1.5), 86 (1), 83 (4), 78 (1.5), 72 (24), 71 (1), 61 (1.2), 56 (4), 55 (2.5), 51 (5), 50 (1), 43 (2), 42 (2.5), 41 (3).

Anal. Calcd for $C_{15}H_{15}N_2O_4Cl_3$: C, 45.77; H, 3.84; N, 7.11. Found: C, 45.88; H, 3.71; N, 7.22.

2-Acetyl-5,5-dimethylpyrazolidin-3-one (5a). Method I. To a solution of 2-acetyl-1-(2,2,2-trichloroethoxycarbonyl)-5,5-dimethylpyrazolidin-3-one (**4a,** 5.0 g, 0.015 mol) in acetic acid (25 ml) under a nitrogen atmosphere was added all at once an equal quantity by weight of zinc dust. Cooling with an ice bath was applied as necessary to prevent any warming. After stirring for 2 hr at room temperature, the mixture was carefully poured into ice-cold water (100 ml) containing K_2CO_3 (70 g). The heterogeneous mixture was extracted well with chloroform which was dried over K_2CO_3. Evaporation of the solvent left an oil which slowly crystallized under high vacuum. Recrystallization of the solid from Et_2O gave 1.40 g (60%) of pure **5a:** mp 67–68°; ir (CCl_4) 3220, 2960, 1750, 1695, 1415, 1375, 1310, 1265, 1240, 1110, 985, 960, 935 cm^{-1}; NMR (CCl_3D) δ 1.31 (s, 6), 2.41 (s, 3), 2.61 (s, 2) 5.22 (broad s, 1, NH); mass spectrum (70 eV) *m/e* (rel intensity) 156 (7, M^+), 115 (4), 114 (47), 100 (7), 99 (100), 83 (8), 82 (2), 72 (7), 71 (3), 56 (8), 55 (6), 43 (22), 42 (8), 41 (9), metastable ion 86; uv (EtOH) 224 nm (ϵ 4290), 248 (2380) shoulder 274 (1290).

Anal. Calcd for $C_7H_{12}N_2O_2$: C, 53.83; H, 7.75; N, 17.94. Found: C, 53.91; H, 7.65; N, 18.02.

Method II. To a solution of 3-benzoxy-1-(2,2,2-trichloroethoxycarbonyl)-5,5-dimethyl-2-pyrazoline (**3f,** 5.00 g, 0.0128 mol) in acetic acid (40 ml) under a nitrogen atmosphere was added all at once an equal quantity by weight of zinc dust. Occasional cooling with an ice bath was necessary to prevent warming. After stirring for 2 hr at room temperature, the mixture was carefully poured into ice-cold water (200 ml) containing K_2CO_3 (150 g). The heterogeneous mixture was then extracted with chloroform which was dried over K_2CO_3 and evaporated to leave a solid. Recrystallization of the solid from Et_2O gave 1.30 g (65%) of pure **5a,** mp 67–68°.

5,5-Dimethyl-2-propionylpyrazolidin-3-one (5b). Method I. Pyrazolidin-3-one **4b** was converted into **5b** in a manner similar to that described for the reaction of **4a** to give **5a.** Recrystallization of the crude product from Et_2O gave a 52% yield of pure **5b:** mp 83.5–84.5°; ir (CCl_4) 3280, 2960, 1750, 1700 (shoulder 1720), 1420, 1380, 1310, 1260, 1225, 1100, 1020, 960, 905 cm^{-1}; NMR (CCl_3D) δ 1.15 (t, J = 8 Hz, 3), 1.35 (s, 6), 2.60 (s, 2), 2.83 (q, J = 8 Hz, 2), 4.95 (broad s, 1, NH); mass spectrum (70 eV) *m/e* (rel intensity) 170 (5, M^+), 115 (3), 114 (32), 100 (5), 99 (100), 83 (6), 72 (5), 57 (13), 56 (5), 55 (3), 42 (5), 41 (6), metastable ion 86; uv (EtOH) 225 nm (ϵ 3900), 246 (2450), shoulder 270 (1500).

Anal. Calcd for $C_8H_{14}N_2O_2$; c, 56.45; H, 8.29; N, 16.46. Found: C, 56.47; H, 8.25; N, 16.25.

Method II. Pyrazoline **3f** in propionic acid was treated with zinc and worked up in a manner similar to the preparation of **5a** by method II. Recrystallization of the crude product from Et_2O gave a 56% yield of pure **5b,** mp 83.5–84.5°.

2-Isobutyryl-5,5-dimethylpyrazolidin-3-one (5c). Method I. Pyrazolidin-3-one **4c** was converted into **5c** in a manner similar to that described for the reaction of **4a** to give **5a.** Column chromatography of the crude product on silicic acid with Et_2O eluent gave a 43% yield of pure **5c:** mp 36–37°; ir (CCl_4) 3260, 2960, 1750, 1690 (shoulder 1710), 1470, 1410, 1390, 1310, 1240, 1220, 1185, 1100, 1050, 995, 970, 910 cm^{-1}; NMR (CCl_3D) δ 1.18 (d, J = 7 Hz, 6), 1.35 (s, 6), 2.66 (s, 2), 3.63 (septet, J = 7 Hz, 1), 5.00 (broad s, 1, NH); mass spectrum (70 eV) *m/e* (rel intensity) 184 (10, M^+), 115 (7), 114 (63), 100 (7), 99 (100), 83 (8), 72 (6), 71 (12), 56 (8), 55 (5), 43 (41), 42 (8), 41 (16), metastable ion 86; uv (EtOH) 226 nm (ϵ 3400), 232 (3000), 250 (2200), shoulder 270 (1450).

Anal. Calcd for $C_9H_{16}N_2O_2$: C, 58.67; H, 8.75; N, 15.21. Found: C, 58.49; H, 9.00; N, 14.98.

Method II. Pyrazoline **3f** in isobutyric acid was treated with zinc and worked up in a manner similar to the preparation of **5a** by method II. Column chromatography of the crude product on silicic acid with Et_2O eluent gave a 40% yield of pure **5c,** mp 36–37°.

5,5-Dimethyl-2-pivaloylpyrazolidin-3-one (5d). Method I. A 60:40 mixture of **3d** and **4d** was converted to **5c** in a manner similar to that described for the reaction of **4a** to give **5a** but using as the solvent a 50:50 mixture of pivalic acid and tetrahydrofuran. Recrystallization of the crude product from Et_2O gave a 34% yield of pure **5d:** mp 97–98°; ir (CCl_4) 3250, 2950, 1750, 1670 (shoulder 1700), 1400, 1310, 1260, 1215, 1175 cm^{-1}; NMR (CCl_3D) δ 1.33 (s, 15), 2.52 (s, 2), 5.06 (broad s, 1, NH); mass spectrum (70 eV) *m/e* (rel intensity) 198 (5, M^+), 183 (2), 127 (2), 115 (5), 114 (61), 100 (7), 99 (100), 85 (3), 83 (7), 72 (5), 57 (35), 56 (8), 55 (5), 42 (7), 41 (19), metastable ion 86; uv (EtOH) 231 nm (ϵ 3300), 239 (2800), 248 (2300), shoulder 275 (1800).

Anal. Calcd for $C_{10}H_{18}N_2O_2$: C, 60.58; H, 9.15; N, 14.13. Found: C, 60.80; H, 8.97; N, 14.32.

Method II. Pyrazoline **3f** in a 50:50 mixture of pivalic acid and tetrahydrofuran was treated with zinc and worked up in a manner similar to the preparation of **5a** by method II. Recrystallization of the crude product from Et_2O gave a 31% yield of pure **5d,** mp 97–98°.

5,5-Dimethyl-2-phenylacetylpyrazolidin-3-one (5e). Pyrazolidin-3-one **4e** was converted into **5e** in a manner similar to that described for the reaction of **4a** to give **5a.** Recrystallization of the crude product from Et_2O gave a 64% yield of pure **5e:** mp 62–63°; ir (CCl_4) 3260, 2960, 1750, 1695, 1420, 1315, 1275, 1235, 1165 cm^{-1}; NMR (CCl_3D) δ 1.29 (s, 6), 2.52 (s, 2), 4.20 (s, 2), 4.90 (broad s, 1, NH), 7.29 (s, 5); mass spectrum (70 eV) *m/e* (rel intensity) 232 (4, M^+, this ion disappears rapidly with time), 214 (2), 149 (2), 118 (6), 115 (7), 114 (100), 113 (5), 100 (5), 99 (86), 91 (37), 83 (23), 72 (28), 71 (9), 65 (7), 56 (20), 55 (15), 42 (9), 41 (17), metastable ion 86; uv (EtOH) end absorption 200 nm (ϵ 11,200), 227 (4400), 248 (2700), shoulder 275 (1350).

Anal. Calcd for $C_{13}H_{16}N_2O_2$: C, 67.22; H, 6.94; N, 12.06. Found: C, 67.01; H, 6.93; N, 12.06.

1-Acetamido-4,4-dimethylazetidin-2-one (9a). From Irradiation of 5a. A solution of 2-acetyl-5,5-dimethylpyrazolidin-3-one (**5a,** 1.56 g, 0.010 mol) in methanol (250 ml) was degassed with a stream of nitrogen for 2 hr, after which it was irradiated for 2 hr with a Hanovia 450-W immersion lamp equipped with a Vycor filter. TLC analysis [silicic acid plates with Et_2O–EtOH (90:10) developer] showed the loss of starting material (detected by uv and I_2) and the appearance of a new spot of slightly smaller R_f (detected by I_2). Stripping of the solvent left an oil which slowly crystallized. Column chromatography of the solid on silicic acid with Et_2O–EtOH (90:10) solvent resulted in the isolation of 1.01 g (65%) of pure **9a:** mp 107–108°; ir (CCl_3H) 3280, 3225 (broad), 2995, 1765, 1705, 1370, 1280, 1225, 1155, 1045, 915, 905 cm^{-1}; NMR (CCl_3D) δ 1.41 (s, 6), 2.01 (s, 3), 2.69 (s, 2); mass spectrum (70 eV) *m/e* (rel intensity) 156 (9, M^+), 138 (4), 115 (7), 114 (93), 101 (14), 100 (30), 99 (45), 83 (32), 82 (18), 72 (53), 57 (15), 56 (61), 55 (55), 44 (15), 43 (100), 42 (12), 41 (75); uv (EtOH) end absorption 200 nm (ϵ 2000).

Anal. Calcd for $C_7H_{12}N_2O_2$: C, 53.83; H, 7.75; N, 17.94. Found: C, 54.03; H, 7.83; N, 17.86.

From Acylation of 22. To a solution of 1-amino-4,4-dimethyl-

azetidin-2-one (**22**, 0.120 g, 1.05 mmol) and triethylamine (0.106 g, 1.05 mmol) in benzene (5 ml) under a nitrogen atmosphere and cooled to 10° was added over a period of 30 min acetyl chloride (0.081 g, 1.05 mmol) in benzene (1 ml). The mixture was then stirred for an additional 30 min at 10° and 5 hr at room temperature. Additional benzene (10 ml) was then added, the mixture was filtered, and the solvent was evaporated to leave 0.145 g (89%) of an oil which was shown to be 90% 1-acetamido-4,4-dimethylazetidin-2-one (**9a**) by TLC and NMR comparison to **9a** obtained from irradiation of **5a**.

4,4-Dimethyl-1-propionylaminoazetidin-2-one (9b). Irradiation of **5b** in methanol, similar to the irradiation described for **5a**, gave after work-up a 36% yield of pure **9b**: mp 100–101°; ir (CCl_3H) 3400, 3250 (broad), 2975, 1765, 1710, 1465, 1375, 1275, 1170 cm^{-1}; NMR (CCl_3D) δ 1.14 (t, J = 8 Hz, 3), 1.42 (s, 6), 2.29 (q, J = 8 Hz, 2), 2.70 (s, 2); camphor depression determined mol wt 189; mass spectrum (70 eV) m/e (rel intensity) 170 (6, M^+), 115 (15), 114 (71), 113 (18), 99 (35), 83 (35), 72 (64), 57 (100), 56 (32), 55 (40), 41 (32); uv (EtOH) end absorption 200 nm (ϵ 2400).

Anal. Calcd for $C_8H_{14}N_2O_2$: C, 56.45; H, 8.29; N, 16.46. Found: C, 56.28; H, 8.16; N, 16.44.

1-Isobutyrylamno-4,4-dimethylazetidin-2-one (9c). Irradiation of **5c** in methanol, similar to the irradiation described for **5a**, gave after work-up a 30% yield of pure **9c**: mp 91–92°; ir (CCl_3H) 3410, 3280 (broad), 2970, 1768, 1706, 1465, 1390, 1375, 1275, 1160 cm^{-1}; NMR (CCl_3D) δ 1.19 (d, J = 7 Hz, 6), 1.42 (s, 6), 2.55 (septet, J = 7 Hz, 1), 2.70 (s, 2); mass spectrum (70 eV) m/e (rel intensity) 184 (7, M^+), 129 (7), 127 (7), 114 (41), 99 (20), 83 (22), 72 (38), 71 (49), 56 (13), 55 (17), 43 (100), 41 (19); uv (EtOH) end absorption 200 nm (ϵ 2200).

Anal. Calcd for $C_9H_{16}N_2O_2$: C, 58.67; H, 8.75; N, 15.21. Found: C, 58.75; H, 8.62; N, 15.25.

4,4-Dimethyl-1-pivaloylaminoazetidin-2-one (9d). Irradiation of **5d** in methanol, similar to the irradiation described for **5a**, gave after work-up a 20% yield of pure **9d**: mp 165.0–165.5°; ir (CCl_3H) 3430, 3290 (broad), 2960, 1768, 1707, 1480, 1460, 1375, 1270, 1160, 1130 cm^{-1}; NMR (CCl_3D) δ 1.28 (s, 9), 1.40 (s, 6), 2.69 (s, 2); mass spectrum (70 eV) m/e (rel intensity) 198 (8, M^+), 183 (1), 167 (1), 155 (1), 143 (5), 141 (4), 114 (19), 99 (21), 85 (13), 83 (28), 72 (43), 57 (100), 56 (11), 55 (12), 42 (5), 41 (21); uv (EtOH) end absorption 200 nm (ϵ 3200).

Anal. Calcd for $C_{10}H_{18}N_2O_2$: C, 60.58; H, 9.15; H, 14.13. Found: C, 60.71; H, 9.40; N, 14.05.

4,4-Dimethyl-1-phenylacetamidoazetidin-2-one (9e). Irradiation of **5e** in methanol, similar to the irradiation described for **5a**, followed by removal of the solvent under reduced pressure at room temperature gave an oil which was shown by VPC analysis to be a complex mixture. Isolated by VPC were **9e, 10, 11, 12, 13,** and **14.** Products **9e, 12, 13,** and **14** are described below while **10** and **11** were identified by comparison of their mass spectra with those of known samples. Products **9e** and **11** were also isolated by column chromatography in yields of 15 and 5%, respectively. Based on an isolated yield of **9e** of 15%, VPC yields of the other products were determined: **10,** 1–2%; **11,** 1–5%; **12,** 10–12%; **13,** 1–2%; **14,** 5–7%.

Irradiation of a nondegassed *tert*-butyl alcohol solution of **5e** through a Corex filter for 3 hr gave, after removal of the solvent, an oil which was shown by VPC to contain mainly **9e** with only small amounts of other products. Column chromatography of the crude reaction mixture gave a 45% isolated yield of **9e.** These conditions represent the best yield of **9e** obtained by us. For **9e:** mp 137–138°; ir (CCl_3H) 3390, 3230 (broad), 2960, 1769, 1700, 1600, 1475, 1370, 1270, 1150 cm^{-1}; NMR (CCl_3D) δ 1.31 (s, 6), 2.61 (s, 2), 3.49 (s, 2), 7.29 (s, 5); mass spectrum (70 eV) m/e (rel intensity) 232 (trace, M^+, this ion disappears rapidly with time), 215 (3), 214 (22), 213 (4), 199 (3), 174 (12), 149 (5), 114 (15), 99 (14), 91 (26), 88 (11), 86 (25), 84 (100), 83 (11), 72 (9), 59 (33), 57 (15), 56 (52), 55 (30), 49 (15), 47 (18), 44 (27), 43 (18), 41 (83); uv (EtOH) end absorption 200 nm (ϵ 12,500), 258 with fine structure (188).

Anal. Calcd for $C_{13}H_{16}N_2O_2$: C, 67.22; H, 6.94; N, 12.06. Found: C, 67.01; H, 6.82; N, 11.73.

2-Benzyl-5,5-dimethylpyrazolidin-3-one (12). Pyrazolidin-3-one **12** was isolated by VPC from the photolyses of **5e** described above. It was identified by comparison of its mass spectrum to that of a sample independently synthesized in our laboratory.[15] For **12:** mass spectrum (70 eV) m/e (rel intensity) 204 (36, M^+), 189 (8), 113 (25), 111 (8), 105 (9), 100 (13), 91 (100), 85 (5), 83 (10), 77 (8), 71 (12), 65 (12), 57 (12), 56 (12), 55 (12), 46 (29), 45 (64), 43 (21), 41 (18).

1,2-Dibenzyl-5,5-dimethylpyrazolidin-3-one (13). Pyrazolidin-3-one **13** was isolated by VPC from the photolyses of **5e** described above. It was identified by comparison of its mass spectrum to that of a sample independently synthesized in our laboratory.[15] For **13:** mass spectrum (70 eV) m/e (rel intensity) 294 (45, M^+), 204 (16), 203 (100), 100 (30), 91 (84), 83 (6), 77 (5), 65 (20), 57 (8), 56 (15), 55 (9), 41 (17).

1-Benzylamino-4,4-dimethylazetidin-2-one (14). β-lactam **14** was isolated by VPC from the photolyses of **5e** described above. It was assigned the structure shown from its mass spectrum. For **14:** mass spectrum (70 eV) m/e (rel intensity) 204 (3, M^+), 190 (28), 175 (12), 118 (19), 113 (6), 99 (7), 92 (14), 91 (100), 90 (10), 72 (40), 41 (8), 65 (20), 57 (7), 56 (10), 55 (12), 42 (7), 41 (10).

1-Amino-4,4-dimethylazetidin-2-one (20). Irradiation of a solution of freshly distilled 5,5-dimethylpyrazolidin-3-one (**1**) in methanol for 20 hr, in a manner similar to the irradiation of **5a** described above, gave, after removal of the solvent at room temperature, an oil. Column chromatography of the oil resulted in the isolation of one product in 15% yield which was identified by its spectra to be **20:** ir (CCl_3H) 3360, 2960, 2940, 1755, 1390, 1385, 1285 cm^{-1}; NMR (CCl_3D) δ 1.38 (s, 6), 2.54 (s, 2), 4.30 (broad s, 2, $-NH_2$); mass spectrum (70 eV) m/e (rel intensity) 114 (15, M^+), 99 (7), 83 (35), 72 (100), 57 (74), 56 (66), 55 (93), 44 (34), 43 (20), 42 (20), 41 (70).

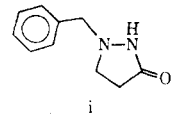
Compound **20** was acetylated to give **9a** for which a correct analysis was obtained (see above, **9a**).

Acknowledgment. We wish to thank the National Institutes of Health (Grant No. AI 10389) for support of this work.

Registry No.—**1,** 42953-82-2; **2,** 49629-15-4; **3a,** 53992-35-1; **3b,** 53992-36-2; **3c,** 53992-37-3; **3d,** 53992-38-4; **3e,** 53992-39-5; **3f,** 49629-16-5; **4a,** 49661-81-6; **4b,** 53992-40-8; **4c,** 53992-41-9; **4d,** 53992-42-0; **4e,** 53992-43-1; **5a,** 49629-18-7; **5b,** 49629-19-8; **5c,** 49629-20-1; **5d,** 49629-21-2; **5e,** 53992-44-2; **9a,** 53992-45-3; **9b,** 53992-46-4; **9c,** 53992-47-5; **9d,** 53992-48-6; **9e,** 53992-49-7; **12,** 53992-50-0; **13,** 53992-51-1; **14,** 53992-52-2; **20,** 53992-53-3.

References and Notes

(1) Presented in part at the 5th Northeast Regional Meeting of the American Chemical Society, Rochester, N.Y., Oct 17, 1973.
(2) For a comprehensive review of synthesis of β-lactams see A. K. Mukerjee and R. C. Srivastava, *Synthesis*, 327 (1973).
(3) (a) E. H. Flynn, "Cephalosporins and Penicillins", Academic Press, New York, N.Y., 1972; (b) M. Manhas and A. K. Bose, "Synthesis of Penicillin, Cephalosporin C and Analogs", Marcel Dekker, New York, N.Y., 1972.
(4) H. T. Clarke, J. R. Johnson, and R. Robinson, "The Chemistry of Penicillin", Princeton University Press, Princeton, N.J., 1949.
(5) (a) D. R. Bender, L. F. Bjeldanes, D. R. Knapp, D. R. McKean, and H. Rapoport, *J. Org. Chem.*, **38,** 3439 (1973); (b) M. F. Chasle and A. Foucaud, *C. R. Acad. Sci., Ser. C,* 2034 (1969).
(6) (a) D. S. C. Black and A. B. Boscacci, *J. Chem. Soc., Chem. Commun.,* 129 (1974); (b) G. Lowe and D. Ridley, *J. Chem. Soc., Perkin Trans. 1,* 2024 (1973); (c) G. Stork and R. Szajewski, *J. Am. Chem. Soc.,* **96,** 5787 (1974); (d) S. N. Ege, *Chem. Commun.,* 759 (1968).
(7) A preliminary account of the photolysis of **9e** has been reported: C. E. Hatch and P. Y. Johnson, *Tetrahedron Lett.,* 2719 (1974).
(8) C. E. Hatch and P. Y. Johnson, *Tetrahedron Lett.,* 2153 (1973).
(9) This reaction with phenylhydrazine gives 2-phenyl-5,5-dimethylpyrazolidin-3-one: B. Prentice, *Justus Liebigs Ann. Chem.,* **292,** 273 (1896).
(10) Abbreviated as TrOC; see T. B. Windholz and D. B. R. Johnson, *Tetrahedron Lett.,* 2555 (1967).
(11) H. Stetter and K. Findeinsen, *Chem. Ber.,* **98,** 3228 (1965).
(12) The failure of **3d,** the *tert*-butyl case, to convert any more than 40% to **4d** leads us to believe this to be an equilibrium process.
(13) In contrast to the acylation of **2,** a 1-acyl-5,5-dimethylpyrazolidin-3-one, a similar acylation of i, a 1-alkylpyrazolidin-3-one, occurs exclusively on nitrogen.[14] Interestingly, acylation under similar conditions of ii, a 1-alkyl-5,5-dimethylpyrazolidin-3-one, gave no apparent reaction: unpublished results from our laboratories.[15]



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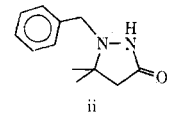
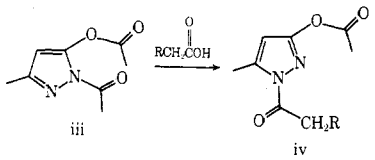


ii

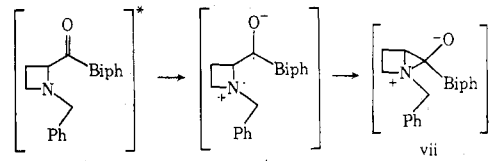
(14) H. Dorn and D. Arndt, *J. Prakt. Chem.,* **313,** 115 (1971).
(15) The synthesis and photolysis of several alkylpyrazolidin-3-ones will be the subject of a forthcoming paper.

(16) This type of mechanism was demonstrated by labeling experiments for the interconversion of *O*- and *N*-acyl isomers in another heterocycle system: A. W. K. Chan and W. D. Crow, *Aust. J. Chem.*, 2967 (1968).
(17) A similar mechanism was set forth for the conversion of iii to iv: K. Arakawa, T. Miyasaka, and H. Ochi, *Chem. Pharm. Bull.*, 214 (1974).



iii iv

(18) *N*-Acylaminoazetidin-2-ones have been previously reported; see E. Testa and L. Fontanella, *Farmaco, Ed. Sci.*, 1017 (1971).
(19) A similar mechanism involving a bicyclo[2.1.0] intermediate, vii, has been proposed in the photolysis of compound v: A. Padwa, F. Albrecht, P. Singh, and E. Vega, *J. Am. Chem. Soc.*, **93**, 2928 (1971).



v* vi vii

(20) Another process which might compete with β-lactam formation is radical cleavage of the relatively weak N–N linkage. Although this mode of reaction has been observed for monoacylhydrazides,[21] 1,1-diacylhydrazides (**5** is a 1,1-diacylhydrazide) have been shown not to undergo this type of reaction.[21]
(21) R. S. Davidson and A. Lewis, *Tetrahedron Lett.*, 4679 (1973).
(22) Product **11** from the photolysis of **5e** in methanol probably occurred by a similar type II mechanism.
(23) A similar 1-aminoazetidin-2-one has been synthesized thermally. See F. D. Greene, R. L. Camp, V. P. Abegg, and G. O. Pierson, *Tetrahedron Lett.*, 4091 (1973).

On the Generation and Reactivity of *N*-Pyrazolyl Radicals in Benzene Solution[1]

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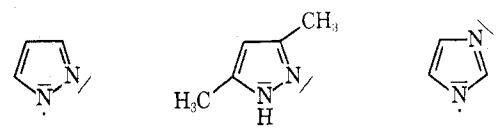
The synthesis of *tert*-butyl 1-pyrazolepercarboxylate (**5a**) and of its 3-methyl derivative **5b** is described. Thermolysis of these compounds in benzene solution at ~140° proceeds predominantly via homolysis and leads to N-phenylated pyrazoles without formation of isomeric *C*-phenyl derivatives. *N*-Pyrazolyl radicals, which are proposed as intermediates, apparently are able to effect homolytic aromatic substitution. Judging from competition with *p*-dichlorobenzene (partial rate factor ~0.25), 1-pyrazolyl (**1**) has a marked electrophilic character. Photolysis of *N*-nitropyrazoles in benzene solution, also leading to N-phenylated derivatives, constitutes an alternative fashion for the generation of *N*-pyrazolyl radicals. Using 3- and 5-substituted pyrazoles as precursors, it is shown that the unpaired electron is delocalized over (at least) the two nitrogen atoms. A σ-type ground state is favored over a π-type electronic structure.

Pyrazolyl radicals—and in general radicals derived from aromatic heterocyclic compounds containing a pyrrole-like nitrogen—can be divided in two classes, viz. (i) radicals which result from homolytic cleavage of a group bound to carbon, and (ii) those formed by such a removal of a substituent on nitrogen. The type i radicals are expected to be closely analogous to homocyclic aryl radicals like phenyl, having the unpaired electron localized in a σ-type orbital.[2] A type ii radical can a priori be compared with both aryl and amino radicals, the latter normally having a π-type electronic ground state.[3]

As an outgrowth of our study on the mechanism of the thermal rearrangement of *N*-nitropyrazoles (resulting in the isomeric 3(5)-nitropyrazoles),[4] we wished to learn about the physical and chemical properties of 1-pyrazolyl (**1**) (Chart I) and its derivatives. To the best of our knowledge **1** is as yet unknown.[5] Recently, Taguchi et al.[6] generated the 4-pyrazolyl radical **2** via decomposition of the parent 4-diazopyrazole in benzene. As anticipated, this type i radical led to the formation of the corresponding 4-phenylpyrazole. A 3,5-diphenyl-1-pyrazolyl radical, thus of type ii, was postulated by Lempert,[7] but there the phenyl rings might strongly influence the character of the radical, as in the well-known polyphenyl substituted pyrryl[8] and imidazolyl[9] radicals.

As regards the electronic ground state of **1**, interaction of the σ orbitals on the two nitrogen atoms has to be considered. Assuming that **1** has C_{2v} symmetry, it may have its unpaired electron in a σ-type orbital, arising from the combination of two N–σ orbitals ($^2B_2$ state); alternatively, the unpaired electron may reside in a π-type orbital involving all five ring atoms ($^2A_2$ or $^2B_1$ state). No information exists about the actual electronic ground state of **1**. For the related 1-imidazolyl (**3**), Evleth et al.[10] predict a $^2B_2$ (σ) ground state, whereas the ESR data of Samuni and Neta[11] strongly point to a π-type electronic structure.

Chart I


1 2 3

In order to shed light on this matter from a theoretical viewpoint, a series of ab initio SCF calculations is now being performed by Mulder et al. (from the Department of Theoretical Organic Chemistry of our laboratory).[12]

The present paper deals with the generation and reactions of **1** and its 3(5)-methylated analog(s). Several attempts to synthesize the peroxides **4a** and **4b** (Chart II) as precursors for **1** were unsuccessful.[13] The preparation of the *tert*-butyl perester **5a** and of its 3-methyl analog **5b** offered no difficulties, however. Here we report on the thermal decomposition of these novel peresters in benzene solution.

Photolytic decomposition of *N*-nitropyrazoles in benzene has also been considered as a source of **1** and derivatives;