(6) Less basic ammonium azide was considered preferable to sodium azide so as not to injure the 5'-ester portions and some other sensitive parts of products and also of the starting material (**1a**). According to our experiences, the former reagent seems to be more soluble in DMF than the latter, and the aqueous washings of the reaction mixtures after evaporation of the reaction solvent usually indicated a practically neutral pH, when equimolar amounts of ammonium chloride and sodium azide were used. The uses of some other soluble azide salts have been described: W. G. Finnegan, R. A. Henry, and R. Lofquist, *J. Am. Chem. Soc.*, **80**, 3908 (1958).
(7) I. L. Doerr, R. J. Cushley, and J. J. Fox, *J. Org. Chem.*, **33**, 1592 (1968).
(8) M. M. Ponpipom and S. Hanesslan, *Can. J. Chem.*, **50**, 250 (1972).
(9) P. A. Levene and R. S. Tipson, *J. Biol. Chem.*, **105**, 419 (1934).
(10) J. F. Codington, I. L. Doerr, and J. J. Fox, *J. Org. Chem.*, **29**, 558 (1964).
(11) This compound has previously been obtained via another route and fully characterized by 100-MHz NMR spectroscopy [D. Wagner, J. P. H. Verheyden, and J. G. Moffatt, *J. Org. Chem.*, **37**, 1876 (1972)]. The shortage of our sample has hampered repeating the measurement at 100 MHz for comparison. The authors are indebted to one of the referees for the information of the above publication.
(12) It must be added that in a trial experiment with **1b** and sodium azide in DMF **3b** was isolated in a low yield from a rather complex mixture.
(13) Measurements after D_2O exchange were also carried out for all the compounds containing labile protons.

Photochemical Formation of Spiro and Bicyclo 1-Acylaminoazetidin-2-ones. Models for the Syntheses of Penicillin-like Systems. II[1]

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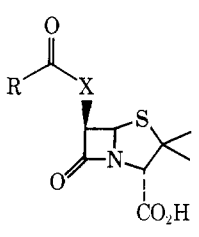
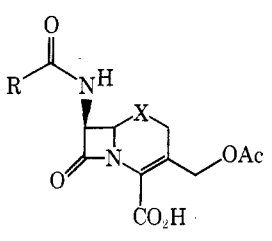
The syntheses and photochemistry of spiro 2-acetylpyrazolidin-3-ones **1d, 2d,** and **13d,** spiro 1-acetylpyrazolidin-3-one **8,** and N-unsubstituted spiro pyrazolidin-3-one **1a** were studied. Upon irradiation these systems were shown to give 1-acetamidoazetidin-2-ones **6, 5, 15, 6,** and 1-aminoazetidin-2-one **7,** respectively, in good yields. A cis-fused bicyclo pyrazolidin-3-one **33a** was also synthesized and irradiated to give bicyclo β-lactam **34a** in 45% isolated yield. β-Lactam **34a** was also synthesized by a second route which involved amination of β-lactam **35a** obtained from the reaction of chlorosulfonyl isocyanate and cyclohexene. The stereochemistry and some reactions of these systems are discussed.

There has been considerable interest in the syntheses of molecules related to the penicillin and cephalosporin antibiotics over the last several decades.[2] During this time many "established" structure–activity relationships concerning these antibiotics have evolved including, among others, the necessity of having the 6-amido group in penicillin (Ia) or the ring sulfur in cephalosporin (IIa) in order to maintain activity. Recent reports on the syntheses of fundamentally different active "penicillin-like" (Ib–d)[3] and "cephalosporin-like" (IIb,c)[4] systems indicate, however, the tentative nature of some of these "established" relationships and the need for continuing studies of different structural analogs of these antibiotics.

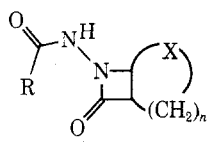


Ia, X = NH, penicillin
b, X = O
c, X = CH_2
d, X = NHNH

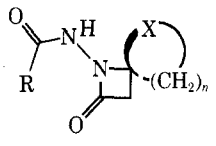


IIa, X = S, cephalosporin
b, X = O
c, X = CH_2

Our interests in this area include approaches to the syntheses of 6-azapenicillins (III, n = 2), 7-azacephalosporins (III, n = 3), and related spiro systems (IV).[5]



III, X = S, CH_2
n = 2, 3



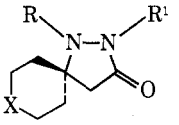
IV, X = S, CH_2
n = 3, 4

Toward these goals we have been examining methods applicable to the synthesis of the *N*-acylaminoazetidin-2-one moiety, which is the dominant feature of both III and IV. Previously we reported on the photochemical rearrangement of monocyclic 2-acyl 5,5-dimethylpyrazolidin-3-ones to give *N*-acylaminoazetidin-2-ones in isolated yields as high as 65%.[1,6] We have now examined the effects of several structural features on this photochemical ring contraction reaction as well as the presence of a remote sulfur atom. This report includes our findings on the syntheses and photochemical reactions of an assortment of 5- and 6-spiro pyrazolidin-3-ones and a 6-fused bicyclo pyrazolidin-3-one as well as the preparation of an *N*-acylaminoazetidin-2-one related to III (X = CH_2) using a procedure which involves amination and acylation of an azetidin-2-one.

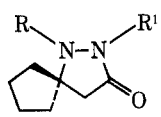
Carbon Spiro Systems. Starting with the known α,β-unsaturated esters, ethyl cyclohexylideneacetate[7] and ethyl cyclopentylideneacetate,[8] carbon spiro systems **1a** and **2a** were prepared by condensation of the respective esters with hydrazine.

While **1a** was obtained in quite good yield, the yield of **2a,** the 5-spiro system, was generally 15–20% lower, presumably because of the increased strain involved in the ring closure step. Both of these acyl hydrazides were solids and were significantly more stable to air oxidation than 5,5-dimethylpyrazolidin-3-one which we had prepared previously.[1] Condensation of either **1a** or **2a** with 2,2,2-trichloroethoxycarbonyl chloride (TrOCCl)[9] under Schotten–Baumann conditions gave 1,2-diacylhydrazides **1b** and **2b,** respectively, in good yields.

Acylation of **1b** or **2b** with acetyl chloride and triethylamine in tetrahydrofuran solvent gave *O*-acyl derivatives **3** and **4,** which were easily rearranged to their corresponding

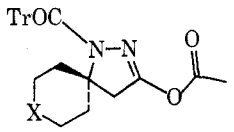


1, X = CH_2; 13, X = S

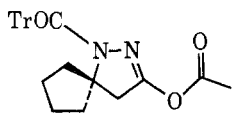


2

a, R = R¹ = H; b, R = TrOC, R¹ = H;
c, R = TrOC, R¹ = CH_3CO; d, R = H, R¹ = CH_3CO



3, X = CH_2; 14, X = S



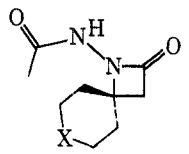
4

N-acyl isomers **1c** and **2c** by heating them neat under nitrogen at 100–120° for 2 hr.

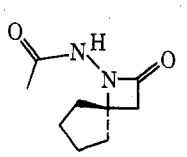
The TrOC protecting group was removed from **1c** and **2c** with zinc dust in acetic acid and the respective 2-acylpyrazolidin-3-ones **1d** and **2d** were extracted from cold aqueous carbonate with chloroform and purified by column chromatography on silicic acid. Sublimation gave **1d** and **2d** analytically pure as low-melting solids. These 5,5-disubstituted 2-acylpyrazolidin-3-ones, which are 1,1-diacylhydrazides, were shown not to rearrange to their 1-acyl isomers upon heating.

It is interesting to compare the ^{13}C chemical shifts of the junction carbon of 6-5 spiro molecules **1a** and **1d** with 5-5 spiro molecules **2a** and **2d** (see Scheme I). We believe that the ca. 10 ppm difference observed for the chemical shift of the junction carbon in these two systems is the result of increased sp^2 character for that carbon in the 5-5 spiro because of its increased strain. This trend continues in the more strained spiro β-lactam (6-4, 5-4) systems (see Experimental Section).

Irradiation of either **1d** or **2d** (see Scheme II) in degassed methanol with a Hanovia 450-W immersion lamp equipped with a Vycor filter for 2 hr gave β-lactams **5** and **6**, respectively, in 50–55% isolated yield. Isolation was performed by column chromatography using silicic acid. The yields of spiro β-lactams **5** and **6** were only slightly lower than those obtained for the monocyclic 5,5-dimethyl system (see Table I).



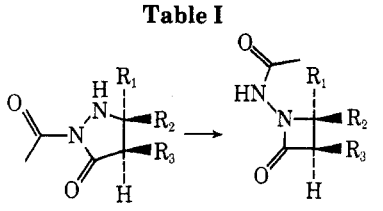
5, X = CH_2; 15, X = S



6

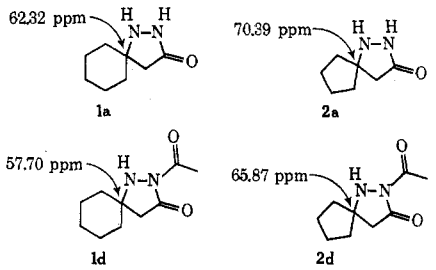
The 6-spiro β-lactam **5** was also obtained in high yield by acetylation of 1-aminoazetidin-2-one **7**, which was prepared by two independent methods. The first involved photolysis of nitrogen unsubstituted pyrazolidin-3-one **1a** for 20 hr in degassed methanol. Column chromatography of the crude photolysis mixture obtained after removal of solvent gave **7** in 15% yield. Amine **7** was found to rearrange at 25° in acidic methanol back to pyrazolidin-3-one **1a**. The second preparation of **7** involved removal of the acetyl group from the exocyclic nitrogen of **5**.[10] Reaction of **5** with 1 equiv of

Table I

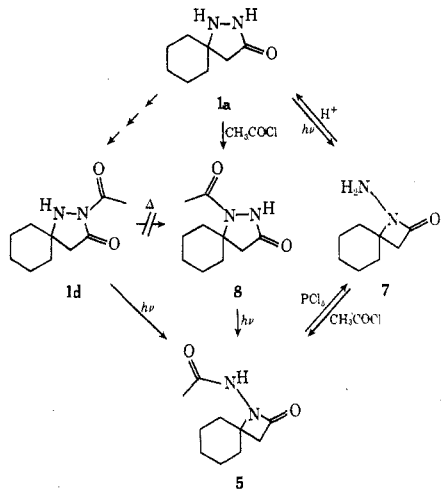


Pyrazolidin-3-one		Azetidin-2-one	R_1	R_2	R_3	Isolated yield of β-lactam, %
	Ref 1		CH_3	CH_3	H	65
			CH_3	H	H	45
2d	–	6	$-(CH_2)_4-$		H	50
1d	–	5	$-(CH_2)_5-$		H	55
13d′	–	15	$-(CH_2)_2S(CH_2)_2-$		H	45
33a	–	34a	H	$-(CH_2)_4-$		45

Scheme I

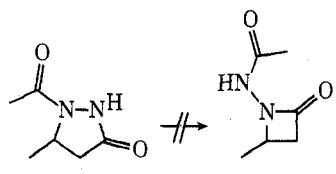


Scheme II



PCl_5 and quinoline in methylene chloride at 25° followed by addition of excess 1-butanol and finally water gave **7** in low yield. No attempt was made to maximize the yield of this reaction.

Interestingly, we found that β-lactam **5** could also be isolated in 30% yield from the photolysis, in degassed methanol for 20 hr, of 1-acetylpyrazolidin-3-one **8**, which was prepared by reaction of **1a** and acetyl chloride. This is the first report of the photochemical ring contraction reaction of a 1-acylpyrazolidin-3-one to give a 1-acylaminoazetidin-2-one. Success of this approach seems to depend at least on the presence of 5,5 disubstitution, since irradiation of 1-acetyl-5-methylpyrazolidin-3-one (**9**) gave no β-lactam **10**. (While not established unambiguously, the aromatic *N*-acetylhydroxypyrazole appears to be the major product in this case.)

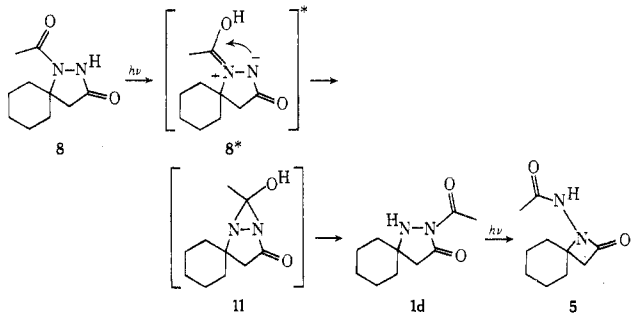


9 10

Scheme III outlines a rationale for the formation of β-lactam **5** from the photolysis of 1-acetylpyrazolidin-3-one **8**. Irradiation of **8** gives **8*** which, upon cyclization, would give the bicyclic intermediate **11**.[11] Rearrangement of **11** to **1d** would be expected to occur occasionally; however, we feel that rearrangement back to **8** should be the predominant reaction of **11** since the "amide type" nitrogen of the hydrazide is the better leaving group. The low concentration of **1d** would account for the long reaction times required for this transformation. The photochemical rearrangement of 2-acylpyrazolidin-3-ones, such as **1d**, to 1-acylaminoazetidin-2-ones has been discussed previously.[1]

Sulfur-Containing Spiro Systems. Sulfur-containing

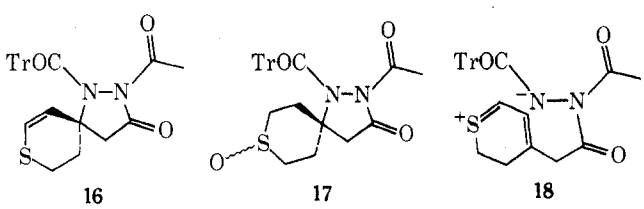
Scheme III



8 8* 11 1d 5

spiro pyrazolidin-3-one **13** was prepared in a manner similar to that described for carbon spiro systems **1** and **2**. The α,β-unsaturated ester, ethyl 4′-thiacyclohexylideneacetate (**12**), was synthesized in good yield via a Horner modification of the Wittig reaction[12] using triethyl phosphonate and thiacyclohexan-4-one.[13] Condensation of the α,β-unsaturated ester with hydrazine gave pyrazolidin-3-one **13a** in moderate yield. Acylation of the 1 position of **13a** with TrOCCl occurred readily to give **13b**, which was treated with acetyl chloride and triethylamine to give the *O*-acyl derivative **14**. Heating **14** neat at 150° for 2 hr gave **13c** in moderate yield. In contrast to the carbon spiro systems, however, the sulfur-containing spiro system **14** turned very dark upon heating. Removal of the protecting group from **13c** to give **13d** required addition of zinc dust in several portions. Only partial removal of the protecting group was observed when the zinc was added in one portion. Presumably sulfur "poisons" the surface of the zinc metal. After its purification by column chromatography, **13d** was irradiated, in a manner similar to that described above for **1a** and **2a**, to give β-lactam **15** in 45% isolated yield. Relative to the carbon spiro systems, the presence of the sulfur atom in system **13** had only a slight lowering effect on the yield of β-lactam (see Table I). That this would be the case was not obvious, since sulfides have been shown to undergo photochemical reaction with carbonyl chromophores via both intra- and intermolecular electron transfer processes.[13,14]

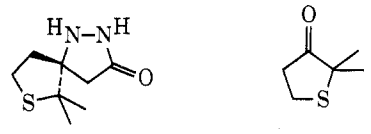
In order to further examine structural modifications related to pyrazolidin-3-one system **13**, thiovinyl ether **16** was synthesized via a Pummerer reaction[15] on sulfoxide **17**. Re-



16 17 18

action of sulfur spiro system **13c** with *m*-chloroperoxybenzoic acid in methylene chloride at 0° gave sulfoxide **17** in 40% yield, probably as a mixture of isomers. Treatment of **17** with refluxing acetic anhydride gave, after work-up, a crude material whose ^{1}H NMR spectra indicated formation of some of the desired thiovinyl ether **16**. However, every effort to purify this material resulted in its decomposition. We feel that the facile decomposition of **16** can be explained in terms of an initial elimination of the good triacyl hydrazide anion to give an unstable diene **18** which would be expected to undergo further decomposition. The orbital alignment of the π bond with the C–N bond of the spiro system should favor such an elimination process.

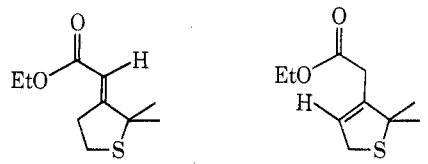
In addition to the sulfur-containing 6-spiro system **13a**, we were also interested in the hindered sulfur-containing



19 21

5-spiro pyrazolidin-3-one **19**. This was to be synthesized from olefin **20** via ketone **21**. Ketone **21** was synthesized from ethyl 2,2-dimethyl-3-thiahexanedioate by Dieckmann cyclization[16] and decarboxylation of the intermediate β-keto ester.

Wittig reaction of ketone **21** with triethyl phosphonoacetate required long reaction times but gave a moderate yield of a mixture of two esters with similar GLC retention times. Ir, ^{1}H NMR, and mass spectral data from GLC collected samples of the two products indicated that they were olefinic esters **20** and **22**. These isomers could be distin-

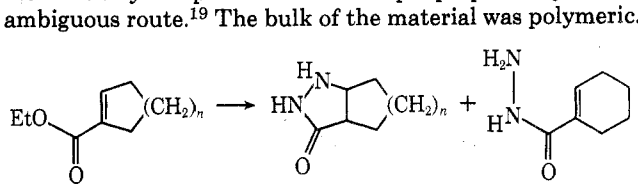


20 22

guished by either their ir or ^{1}H NMR spectra. The α,β-unsaturated ester **20** had a carbonyl band in its ir spectrum at 1707 cm^{-1}, while the β,γ-unsaturated isomer **22** had a carbonyl band in its ir spectrum at 1731 cm^{-1}. The ^{1}H NMR spectrum of **20** contained two triplet absorptions with coupling constants of 7 Hz, one of which was also coupled to the vinyl proton as determined by double resonance, while the ^{1}H NMR spectra of **22** had absorptions for the two methylene groups with only fine coupling. It is interesting to note that the olefinic proton absorptions of **20** and **22** have the same chemical shift. The presence of only the *E* isomer of **20** is not surprising, since the Wittig reaction is known to be affected by steric factors.[12]

Because of the difficulty in the separation of esters **20** and **22**, hydrazine was condensed with a mixture of the two. Reaction under a variety of conditions produced, however, only intractable material from which no product with the properties expected for **19** could be isolated.

Carbon Bicyclo Systems. Although a large number of monocyclic pyrazolidin-3-ones have been prepared, a search of the literature reveals no examples of a nitrogen-unsubstituted pyrazolidin-3-one ring fused to another ring. We therefore prepared the two cyclic α,β-unsaturated esters 1-ethoxycarbonylcyclopent-1-ene (**23**)[17] and 1-ethoxycarbonylcyclohex-1-ene (**24**)[18] in order to examine their reactions with hydrazine. From reaction of the cyclopentene system with hydrazine under a variety of conditions we were unable to isolate any products with the properties expected for bicyclo compound **25**. In contrast, from the reaction of the cyclohexene system with 1 equiv of hydrazine at 120° for 6 hr we were able to obtain, after column chromatography, a low yield (5–10%) of the desired bicyclo pyrazolidin-3-one **26**. Also isolated from this reaction was a small amount of the α,β-unsaturated hydrazide **27** which was identified by comparison with a sample prepared by an unambiguous route.[19] The bulk of the material was polymeric.



23, $n = 1$ **25**, $n = 1$ **27**
24, $n = 2$ **26**, $n = 2$

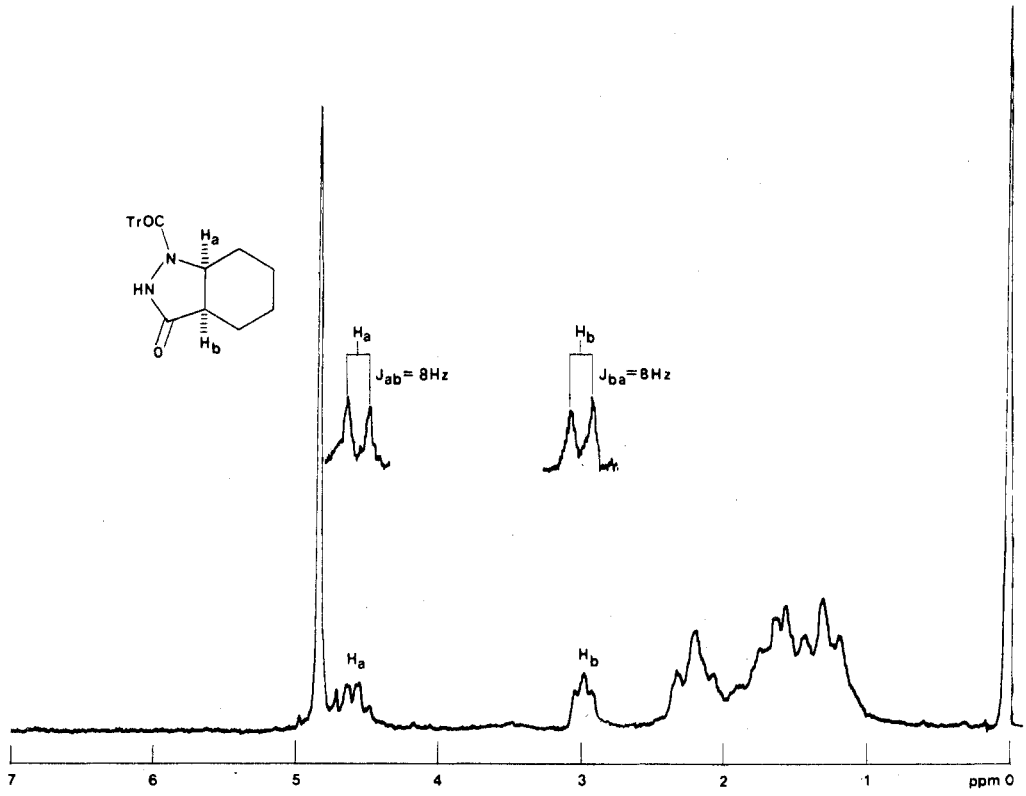


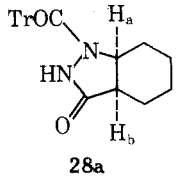
Figure 1. ^1H NMR spectrum of *cis*-1-(2,2,2-trichloroethoxycarbonyl)indazolidin-3-one (**28a**) in CCl_3D at room temperature. Inserts are the absorptions of the bridgehead protons decoupled from the corresponding adjacent methylene (for H_a, $H_2 \approx 210$ Hz; H_b, $H_2 \approx 160$ Hz).

These results on the hydrazine condensation of esters **23** and **24** indicate that pyrazolidin-3-one formation by this method is strongly affected by the strain of a fused ring and does not represent a good approach to systems like **26.**

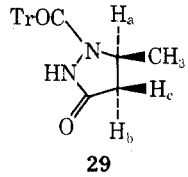
Although we were able to obtain **26** pure off a column, the best yields of 1-acylated **26** were obtained by using partially purified material (see Experimental Section). Acylation of partially purified **26** with TrOCCl gave a product which was determined by ^{13}C NMR to be mainly one diastereomer of **28** containing some of the other diastereomer. Recrystallization removed the minor isomer. The identity of the major isomer was determined to be the desired *cis*-**28** (**28a**) by comparison of its ^1H NMR spectra with the ^1H NMR spectra of compound **29** (see Figures 1 and 2). After correction for the methine vs. methylene difference, H_a and H_b in **29** have the same chemical shifts as the two bridgehead protons of **28a,** while the absorption for H_c in **29** is upfield. Also the coupling constant of the two bridgehead protons of **28a** is the same as the two "cis" (H_a, H_b) protons in **29.**

The isolation of predominantly **28a** from acylation of the cis/trans **26** (**26a,b**) mixture indicates that the predominant isomer formed in the hydrazine condensation was probably **26a** (^{13}C NMR data indicated that one major diastereomer was formed). Formation of predominantly **26a** can be rationalized by favored axial protonation of intermediate **30** which can close to give the cis product.[20]

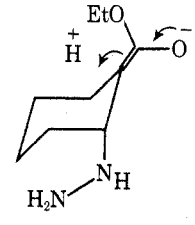
Reaction of **28a,** which is a 5-monosubstituted pyrazolidin-3-one, with acetyl chloride and triethylamine in tetrahydrofuran gave a 70:30 mixture of *N*-acetyl *cis*-**31** (**31a**)



28a



29



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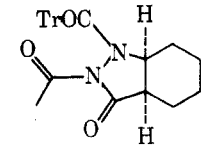
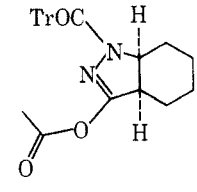


31a

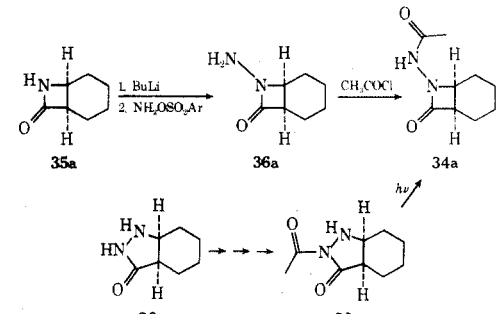


32a

and *O*-acetyl *cis*-**32** (**32a**) isomers. This is in contrast with the behavior of the 5,5-disubstituted pyrazolidin-3-ones **1b, 2b,** and **13b,** which, when acylated under similar conditions, gave exclusively *O*-acyl derivatives. Heating the mixture of **31a** and **32a** at 110° for 3 hr gave pure *N*-acetyl **31a.** Removal of the protecting group from **31a** with zinc gave *cis*-**33** (**33a**) (see Scheme IV). Irradiation of **33a** gave *cis*-**34** (**34a**), which was isolated by column chromatography in 45% yield. The presence of a fused six-membered ring apparently has only a small effect on the photochemical ring contraction reaction (see Table I).

β-Lactam **34a** was also prepared from N-unsubstituted β-lactam *cis*-**35** (**35a**),[21] which was prepared by reaction of chlorosulfonyl isocyanate with cyclohexene followed by re-

Scheme IV



35a **36a** **34a**

26a **33a**

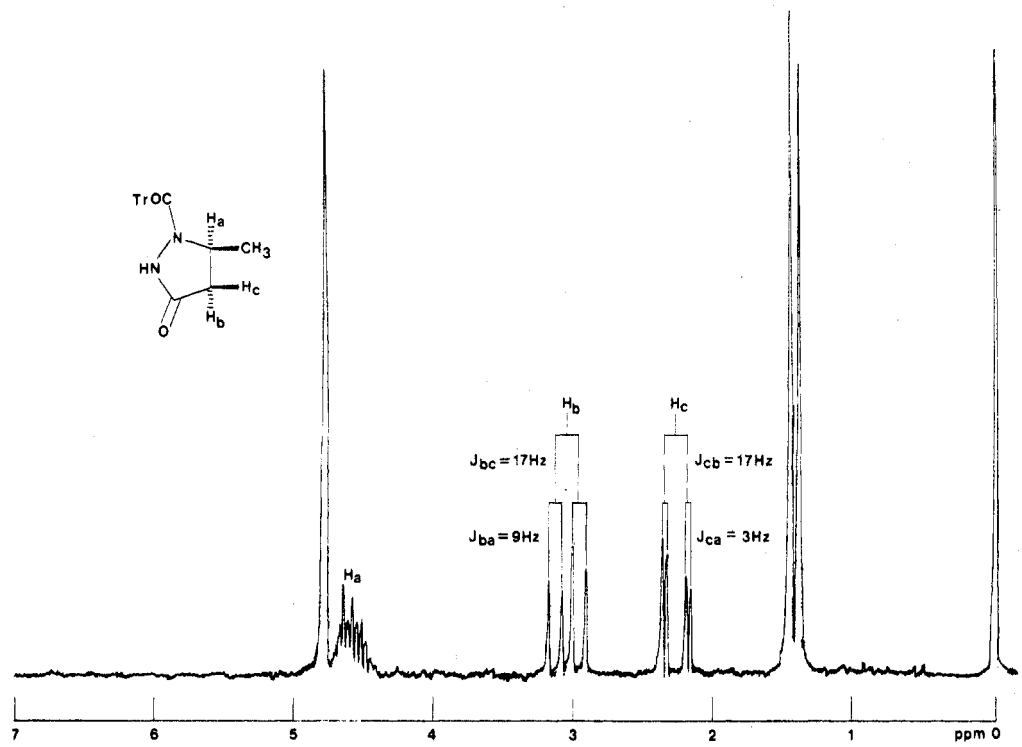


Figure 2. ^{1}H NMR spectrum of 1-(2,2,2-trichloroethoxycarbonyl)-5-methylpyrazolidin-3-one (**29**) in CCl_3D at room temperature.

moval of the chlorosulfonyl moiety with NaOH–Na_2SO_3.[22] Amination of the anion of **35a** with 1 equiv of *O*-mesitylene sulfonylhydroxylamine[23] resulted in 1-amino β-lactam *cis*-**36** (**36a**). Acylation of **36a**, using conditions similar to those used for the acylation of 1-amino β-lactam **10**, gave **34a** which was identical by ir, ^{1}H NMR, and TLC with the photoproduct of **33a**.

Further studies on systems of the generalized structure III are underway in our laboratories and will be reported at a later time.

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 457A spectrometer. The ^{1}H 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. The ^{13}C NMR spectra were taken on a Varian CFT-20 spectrometer and are reported in parts per million downfield from tetramethylsilane. The abbreviations s, singlet; d, doublet; t, triplet, q, quartet refer to the multiplicity of the absorption in an off-resonance decoupled spectrum. 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- 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. Irradiations were carried out using a Hanovia 450-W immersion lamp equipped with a Vycor filter unless otherwise specified.

Pyrazolidin-3-one-5-spirocyclohexane (1a). To 95% hydrazine (3.05 g, 89.5 mmol) cooled to 0° under a nitrogen atmosphere was added dropwise ethyl cyclohexylideneacetate[7] (15.00 g, 89.5 mmol). After the addition was complete, the mixture was allowed to warm to room temperature and to stir for 1 hr. The mixture was then heated at 120° for 6 hr. Immediately after removing the oil bath aspirator vacuum was applied to the reaction vessel to remove the ethanol formed. When the reaction vessel had cooled to room temperature, it was placed under high vacuum. The crude solid (13.7 g, 99%) obtained from this procedure was acylated directly without further purification. An analytical sample was obtained by recrystallization from ethanol. For **1a**: mp 138–140°; ir (CCl_3H) 3430, 3230 (broad), 2930, 2855, 1700 (broad), 1450, 1380, 1310, 1110, 990, 950, 880 cm^{-1}; ^{1}H NMR (CCl_3D) δ 1.20–1.85 (m, 10), 2.30 (s, 2); ^{13}C NMR (CCl_3D) δ 22.70 (t), 25.57 (t), 43.33 (t), 62.32 (s), 178.00 (s); mass spectrum (70 eV) *m/e* (rel intensity) 154 (43, M^+), 139 (4), 125 (7), 123 (19), 112 (25), 111 (100), 98 (61), 97 (10), 96 (8), 95 (24), 83 (14), 81 (20), 79 (10), 68 (12), 67 (26), 55 (22), 54 (13), 53 (11), 41 (28); uv (EtOH) 203 nm (ε 3900), shoulder 219 (2100).

Anal. Calcd for $C_8H_{14}N_2O$: C, 62.31; H, 9.15; N, 18.17. Found: C, 62.11; H, 9.08; N, 18.10.

1-(2,2,2-Trichloroethoxycarbonyl)pyrazolidin-3-one-5-spirocyclohexane (1b). To a solution of crude pyrazolidin-3-one-5-spirocyclohexane (**1a**, 13.7 g, 89.0 mmol) in a mixture of aqueous 2 *N* NaOH (45 ml) and tetrahydrofuran (45 ml) cooled to 10–20° under a nitrogen atmosphere was added dropwise 2,2,2-trichloroethoxycarbonyl chloride (18.8 g, 89.0 mmol). After the addition was complete, the mixture was allowed to warm to room temperature and to stir for 2 hr. The precipitate which formed during the reaction was filtered off and washed with a little water. Recrystallization of the solid from ethanol gave 16.5 g (57%) of pure **1b**: mp 193–194°; ir (CCl_3H) 3410, 2940, 2860, 1710 (broad), 1450, 1390, 1340, 1300, 1140, 910 cm^{-1}; ^{1}H NMR (CCl_3D) δ 1.00–2.60 (m, 10), 2.76 (s, 2), 4.84 (s, 2); mass spectrum (70 eV) *m/e* (rel intensity) 328 (6, 3-Cl, M^+), 207 (6), 181 (6), 154 (10), 153 (8), 123 (25), 122 (43), 111 (25), 98 (22), 97 (16), 96 (26), 95 (100), 94 (43), 81 (57), 79 (21), 68 (23), 67 (54), 61 (22), 55 (35), 54 (26), 44 (43), 41 (39).

Anal. Calcd for $C_{11}H_{15}N_2O_3Cl_3$: C, 40.08; H, 4.59; N, 8.56. Found: C, 39.90; H, 4.64; N, 8.42.

2-Acetyl-1-(2,2,2-trichloroethoxycarbonyl)pyrazolidin-3-one-5-spirocyclohexane (1c) via 3-Acetoxy-1-(2,2,2-trichloroethoxycarbonyl)-2-pyrazoline-5-spirocyclohexane (3). To a solution of 1-(2,2,2-trichloroethoxycarbonyl)pyrazolidin-3-one-5-spirocyclohexane (**1b**, 16.5 g, 50.1 mmol) and triethylamine (5.10 g, 50.1 mmol) in tetrahydrofuran (300 ml) at room temperature under a nitrogen atmosphere was added dropwise over a period of 30 min acetyl chloride (3.95 g, 40.1 mmol). 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. ^{1}H NMR analysis revealed this to be the O-acylated product **3**: ^{1}H NMR (CCl_3D) δ 1.00–2.00 (m, 10), 2.28 (s, 3), 3.13 (s, 2), 4.87 (s, 2).

Without further purification the O-acylated material was heated neat under a nitrogen atmosphere at 110° for 3 hr. Upon cooling was obtained a white solid which upon recrystallization from Et_2O gave 14.6 g (73%) of pure **1c**: mp 117.5–118.5°; ir (CCl_3H) 2940, 2860, 1740 (broad), 1500, 1370, 1260, 970 cm^{-1}; ^{1}H NMR (CCl_3D) δ 1.10–2.40 (m, 10), 2.52 (s, 3), 2.76 (s, 2), 4.79 (s, 2); mass spectrum

(70 eV) *m/e* (rel intensity) no parent, 326 (trace, 3-Cl), 293 (trace, 3-Cl), 271 (trace, 3-Cl), 154 (13), 140 (12), 122 (6), 111 (18), 98 (22), 97 (20), 96 (25), 81 (48), 68 (22), 67 (45), 61 (30), 60 (57), 55 (25), 54 (26), 45 (92), 44 (98), 43 (100), 42 (51), 41 (39).

Anal. Calcd for $C_{13}H_{17}N_2O_4Cl_3$: C, 42.01; H, 4.61; N, 7.54. Found: C, 42.04; H, 4.56; N, 7.57.

2-Acetylpyrazolidin-3-one-5-spirocyclohexane (1d). To a solution of 2-acetyl-1-(2,2,2-trichloroethoxycarbonyl)pyrazolidin-3-one-5-spirocyclohexane (**1c**, 5.00 g, 13.5 mmol) in acetic acid (30 ml) at room temperature 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 (120 ml) containing K_2CO_3 (90 g). The heterogeneous mixture was extracted well with chloroform, which was evaporated to leave an oil. Column chromatography of the oil on silicic acid with Et_2O eluent gave 1.59 g (60%) of a colorless oil which was shown to be pure **1d:** ir (CCl_3H) 3280, 2930, 2855, 1749, 1700, 1412, 1375, 1310, 1280, 970, 905 cm^{-1}; ^1H NMR (CCl_3D) δ 1.30–1.90 (m, 10), 2.48 (s, 6), 2.64 (s, 2), 4.44 (broad s, 1, NH); ^{13}C NMR (CCl_3D) δ 22.70 (t), 24.00 (q), 25.53 (t), 35.52 (t), 45.51 (t), 57.72 (s), 167.50 (s), 173.01 (s); mass spectrum (70 eV) *m/e* (rel intensity) 196 (7, M^+), 178 (3), 155 (8), 154 (75), 125 (7), 112 (46), 111 (100), 98 (94), 97 (13), 95 (8), 81 (11), 79 (8), 68 (7), 67 (14), 58 (8), 55 (13), 54 (8), 53 (9), 43 (57), 41 (26); uv (EtOH) 226 nm (ϵ 3800), 240 (2750).

Anal. Calcd for $C_{10}H_6N_2O_2$: C, 61.20; H, 8.22; N, 14.27. Found: C, 60.95; H, 8.03; N, 14.26.

1-Acetamidoazetidin-2-one-4-spirocyclohexane (5). From Irradiation of 1d. A solution of 2-acetylpyrazolidin-3-one-5-spirocyclohexane (**1d**, 1.30 g, 6.65 mmol) in methanol (250 ml) was degassed with a stream of nitrogen for 2 hr, after which it was irradiated for 2 hr. TLC analysis [silicic acid plates with Et_2O–EtOH (90:10 mixture by volume) 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 mixture by volume) eluent resulted in the isolation of 0.705 g (55%) of a white solid which was shown to be pure **5**: mp 147.5–148.5°; ir (CCl_3H) 3410, 2935, 2860, 1769, 1710, 1455, 1370, 1305, 1090, 997 cm^{-1}; ^1H NMR (CCl_3D) δ 1.00–1.92 (m, 10), 2.00 (s, 3), 2.60 (s, 2), 8.90 (broad s, 1, NH); ^{13}C NMR (CCl_3D) δ 20.71 (q), 24.10 (t), 25.02 (t), 34.43 (t), 45.42 (t), 65.90 (s), 168.01 (s), 170.02 (s); mass spectrum (70 eV) *m/e* (rel intensity) 196 (9, M^+), 178 (11), 154 (40), 123 (16), 122 (78), 112 (18), 111 (37), 100 (23), 98 (40), 96 (37), 95 (73), 94 (33), 81 (100), 79 (43), 75 (50), 68 (42), 67 (88), 56 (23), 55 (56), 54 (40), 53 (31), 43 (89), 41 (55).

Anal. Calcd for $C_{10}H_{16}N_2O_2$: C, 61.20; H, 8.22; N, 14.27. Found: C, 61.09; H, 8.34; N, 14.20.

From Irradiation of 8. A solution of 1-acetylpyrazolidin-3-one-5-spirocyclohexane (**8**, 0.100 g, 0.50 mmol) in methanol (40 ml) was degassed with a stream of nitrogen for 2 hr, after which it was irradiated for 20 hr. Stripping of the solvent left an oil. Column chromatography of the oil on silicic acid with Et_2O–EtOH (90:10 mixture by volume) eluent resulted in 0.031 g (31%) of a solid. The solid was shown to be pure **5** by ir, TLC, and ^1H NMR comparison to **5** obtained from the irradiation of **1d**.

From Acylation of 7. To a solution of 1-aminoazetidin-2-one-4-spirocyclohexane (**7**, 0.023 g, 0.15 mmol) and triethylamine (0.016 g, 0.15 mmol) in benzene (1 ml) under a nitrogen atmosphere and cooled to 10° was added slowly acetyl chloride (0.012 g, 0.15 mmol). After the addition was complete, the mixture was stirred for 1 hr at 10° and 5 hr at room temperature. Additional benzene (5 ml) was added, the mixture was filtered, and the solvent was evaporated to leave an oil which was shown to be 95% 1-acetamidoazetidin-2-one-4-spirocyclohexane (**5**) by ir, ^1H NMR, and TLC comparison to **5** obtained from the irradiation of **1d**.

Pyrazolidin-3-one-5-spirocyclopentane (2a). Compound **2a** was prepared in 90% yield in a manner similar to that described for **1a**. For **2a:** mp 95–97°; ir (CCl_3H) 3430, 3225 (broad), 2945, 2865, 1702 (broad), 1455, 1375, 1339, 1080, 962, 880 cm^{-1}; ^1H NMR (CCl_3D) δ 1.55–1.90 (m, 8), 2.48 (s, 2); ^{13}C NMR (CCl_3D) δ 24.04 (t), 37.08 (t), 43.51 (t), 70.39 (s), 178.04 (s); mass spectrum (70 eV) *m/e* (rel intensity) 140 (23, M^+), 111 (37), 109 (18), 108 (9), 98 (100), 97 (21), 82 (21), 81 (11), 68 (31), 58 (15), 41 (29).

Anal. Calcd for $C_7H_{12}N_2O$: C, 59.98; H, 8.63; N, 19.98. Found: C, 59.92; H, 8.56; N, 19.93.

1-(2,2,2-Trichloroethoxycarbonyl)pyrazolidin-3-one-5-spirocyclopentane (2b). Compound **2b** was prepared in 41% yield in a manner similar to that described for **1b**. For **2b:** mp 196–197°; ir (CCl_3H) 3400, 2945, 2865, 1709 (broad), 1450, 1385, 1340, 1285, 1130 cm^{-1}; ^1H NMR (CCl_3D) δ 1.5–2.10 (m, 6), 2.30–2.65 (m, 2), 2.75 (s, 2), 4.86 (s, 2); mass spectrum (70 eV) *m/e* (rel intensity) 314 (5, 3-Cl, M^+), 167 (8), 139 (16), 131 (10, 3-Cl), 111 (15), 109 (31), 108 (49), 98 (27), 97 (23), 96 (29), 95 (15), 81 (28), 80 (88), 79 (27), 78 (21), 77 (17), 68 (17), 67 (100), 61 (35), 55 (23), 54 (31), 53 (20), 44 (67), 41 (47).

Anal. Calcd for $C_{10}H_{13}N_2O_3Cl_3$: C, 38.06; H, 4.15; N, 8.88. Found: C, 38.06; H, 4.18; N, 8.81.

2-Acetyl-1-(2,2,2-trichloroethoxycarbonyl)pyrazolidin-3-one-5-spirocyclopentane (2c) via 3-Acetoxy-1-(2,2,2-trichloroethoxycarbonyl)-2-pyrazoline-5-spirocyclopentane (4). Compound **2c** was prepared in 66% yield via compound **4** in a manner similar to that described for **1c** and **3**. For **4:** ^1H NMR (CCl_3D) δ 1.45–2.10 (m, 6), 2.26 (s, 3), 2.35–2.70 (m, 2), 3.16 (s, 2), 4.90 (s, 2). For **2c:** mp 87.5–88.5°; ir (CCl_3H) 2955, 1740 (broad), 1450, 1370, 1260, 1155, 1115, 970 cm^{-1}; ^1H NMR (CCl_3D) δ 1.50–2.10 (m, 6), 2.15–2.45 (m, 2), 2.53 (s, 3), 2.77 (s, 2), 4.80 (s, 2); mass spectrum (70 eV) *m/e* (rel intensity) no parent, 312 (trace, 3-Cl), 280 (trace, 3-Cl), 238 (trace, 3-Cl), 225 (3), 182 (1), 140 (12), 114 (12), 111 (8), 99 (10), 98 (30), 96 (14), 86 (10), 82 (23), 81 (14), 79 (9), 67 (60), 61 (17), 60 (100), 54 (16), 45 (94), 44 (91), 43 (96).

Anal. Calcd for $C_{12}H_{15}N_2O_4Cl_3$: C, 40.30; H, 4.23; N, 7.83. Found: C, 40.22; H, 4.28; N, 7.72.

2-Acetylpyrazolidin-3-one-5-spirocyclopentane (2d). Compound **2d** was prepared in 51% yield in a manner similar to that described for **1d**. For **2d:** mp 69–71°; ir (CCl_3H) 3260, 2925, 2870, 1750, 1700, 1410, 1375, 1340, 1290, 975, 840 cm^{-1}; ^1H NMR (CCl_3D) δ 1.50–1.95 (m, 8), 2.44 (s, 3), 2.74 (s, 2), 5.06 (broad s, 1, NH); ^{13}C NMR (CCl_3D) δ 23.96 (q), 37.22 (t), 45.83 (t), 65.87 (s), 167.00 (s), 172.40 (s); mass spectrum (70 eV) *m/e* (rel intensity) 182 (10, M^+), 141 (9), 140 (100), 112 (12), 111 (59), 109 (8), 99 (12), 98 (84), 97 (32), 82 (17), 81 (14), 79 (11), 67 (43), 60 (23), 54 (22), 45 (21), 44 (18), 43 (50), 41 (32); uv (EtOH) 225 nm (ϵ 3700), 244 (2250).

Anal. Calcd for $C_9H_{14}N_2O_2$: C, 59.32; H, 7.74; N, 15.37. Found: C, 59.27; H, 7.68; N, 15.35.

1-Acetamidoazetidin-2-one-4-spirocyclopentane (6). Compound **6** was prepared in 50% yield in a manner similar to that described for **5**. For **6**: mp 95–96°; ir (CCl_3H) 3400, 2950, 2870, 1769, 1710, 1453, 1368, 1333, 1091, 907 cm^{-1}; ^1H NMR (CCl_3D) δ 1.40–2.00 (m, 8), 2.00 (s, 3), 2.79 (s, 2), 9.14 (broad s, 1, NH); ^{13}C NMR (CCl_3D) δ 20.59 (q), 24.12 (t), 33.91 (t), 47.21 (t), 71.53 (s), 168.51 (s), 170.00 (s); mass spectrum (70 eV) *m/e* (rel intensity) 182 (2, M^+), 164 (44), 163 (33), 149 (6), 140 (10), 121 (6), 111 (9), 108 (8), 100 (15), 98 (32), 83 (11), 82 (35), 81 (23), 80 (12), 79 (24), 67 (100), 62 (31), 61 (13), 60 (12), 59 (27), 58 (12), 44 (13), 43 (35), 41 (32).

Anal. Calcd for $C_9H_{14}N_2O_2$: C, 59.32; H, 7.74; N, 15.37. Found: C, 59.13; H, 7.58; N, 15.26.

1-Aminoazetidin-2-one-4-spirocyclohexane (7). From Irradiation of 1a. A solution of freshly recrystallized pyrazolidin-3-one-5-spirocyclohexane (**1d**, 1.00 g, 6.50 mmol) in methanol (250 ml) was degassed with a stream of nitrogen for 2 hr after which it was irradiated for 20 hr. Stripping of the solvent left an oil which was column chromatographed on silicic acid with Et_2O–EtOH (80:20 mixture by volume) eluent. From the column was obtained 0.171 g (17%) of an oil which was identified from its spectra to be **7**: ir (CCl_3H) 2920, 1745, 1300, 1000, 905 cm^{-1}; ^1H NMR (CCl_3D) δ 1.10–2.10 (m, 10), 2.48 (s, 2), 3.80 (broad s, 2, NH_2); ^{13}C NMR (CCl_3D) δ 24.08 (t), 24.93 (t), 33.33 (t), 45.68 (t), 62.80 (s), 167.59 (s); mass spectrum (70 eV) *m/e* (rel intensity) 154 (35, M^+), 151 (12), 139 (16), 138 (14), 123 (34), 122 (100), 111 (15), 110 (25), 99 (16), 96 (18), 95 (84), 94 (23), 81 (55), 79 (26), 68 (21), 67 (51), 55 (45), 54 (26), 41 (34).

Compound **7** was acetylated to give **5**, for which a correct analysis was obtained (see above, **5**).

From Deacylation of 5. To a solution of PCl_5 (0.470 g, 2.2 mmol) and quinoline (0.516 g, 4 mmol) in methylene chloride (20 ml) cooled to 0° under a nitrogen atmosphere was added slowly a solution of 1-acetamidoazetidin-2-one-4-spirocyclohexane (**5**, 0.370 g, 1.9 mmol) in methylene chloride (1 ml). After the addition was complete, the mixture was allowed to warm to room temperature and to stir for 2 hr. The mixture was then cooled to 0° and *n*-BuOH (2.96 g, 40 mmol) was added dropwise. After the addition was complete, the mixture was allowed to warm to room temperature and to stir for 2 hr. After cooling the solution to 0° NaCl-saturated water (20 ml) was added dropwise. The mixture was stirred at 0° for 2 hr, after which the organic and aqueous layers were separated. The aqueous layer was extracted with methylene chloride and the combined organic layers washed with aqueous 2 *N* NaOH and dried over anhydrous K_2CO_3. Evaporation of the solvent left

an oil which was column chromatographed on silicic acid with Et_2O–EtOH (80:20 mixture by volume) eluent. From the column was isolated 0.045 g (15%) of an oil which was shown to be **7** by ir, ^1H NMR, and TLC comparison to **7** obtained from the photolysis of **1a**.

1-Acetylpyrazolidin-3-one-5-spirocyclohexane (8). To a solution of pyrazolidin-3-one-5-spirocyclohexane (**2a**, 1.54 g, 0.010 mol) and triethylamine (0.79 g, 0.010 mol) in methylene chloride (20 ml) cooled to 0° under a nitrogen atmosphere was added acetyl chloride (1.01 g, 0.010 mol) over a period of 15 min. The resultant mixture was stirred for 4 hr at 0° and 12 hr at room temperature after which it was heated to boiling and the insoluble triethylamine hydrochloride salt was filtered off. Evaporation of the benzene left a white solid. Recrystallization from Et_2O gave 0.571 g (29%) of pure **8**: mp 175.0–176.0°; ir (CCl_3H) 3385, 2915, 1707, 1630, 1382, 1300, 1270, 980 cm^{-1}; ^1H NMR (CCl_3D) δ 1.08–1.52 (m, 3), 1.60–2.04 (m, 5), 2.20 (s, 3), 2.20–2.64 (m, 2), 2.78 (s, 2); ^{13}C NMR (CCl_3D) δ 22.93 (q), 23.25 (t), 24.72 (t), 34.17 (t) 42.88 (t), 66.83 (s), 162.91 (s), 167.90 (s); mass spectrum (70 eV) *m/e* (rel intensity) 196 (30, M^+), 154 (100), 122 (21), 112 (24), 111 (69), 101 (24), 98 (65), 86 (100), 81 (31), 67 (22), 58 (25), 57 (27), 55 (27), 43 (46), 41 (31); uv (EtOH) 239 nm (ϵ 11000).

Anal. Calcd for $C_{10}H_{16}N_2O_2$: C, 61.20; H, 8.22; N, 14.27. Found: C, 61.46; H, 8.38; N, 14.08.

1-Acetyl-5-methylpyrazolidin-3-one (9). Compound **9** was prepared in 24% yield from 5-methylpyrazolidin-3-one[24] in a manner similar to that described for **8**. For **9**: mp 138.5–139.5°; ^1H NMR (CCl_3D) δ 1.40 (d, J = 6 Hz, 3), 2.11 (s, 3), 2.28 (d, J = 17 Hz, 1), 3.14 (doublet of doublets, J = 9 and 17 Hz, 1), 4.34–4.82 (m, 1), 10.52 (broad s, 1, NH); ^{13}C NMR (CCl_3D) δ 19.48 (q), 20.67 (q), 39.00 (t), 52.59 (d), 161.89 (s), 168.92 (s); mass spectrum (70 eV) *m/e* (rel intensity) 142 (16, M^+), 100 (64), 85 (32), 69 (35), 58 (29), 57 (23), 43 (100); uv (EtOH) 238 nm (ϵ 9800).

Anal. Calcd for $C_6H_{10}N_2O_2$: C, 50.69; H, 7.09; N, 19.71. Found: C, 50.64; H, 7.01; N, 19.61.

Ethyl 4′-Thiacyclohexylideneacetate (12). To a mixture of 57% dispersion of sodium hydride in mineral oil (4.2 g, 0.100 mol) in dry benzene (50 ml) under a nitrogen atmosphere was added dropwise over a 45-min period triethyl phosphonoacetate (23.5 g, 0.105 mol). Cooling was applied as necessary to keep the temperature below 35°. After the addition of the triethyl phosphonoacetate was complete, the almost clear solution was stirred for 1 hr at room temperature. To this preformed anion was added thiacyclohexan-4-one[13] (11.6 g, 0.100 mol) over a 45-min period. Cooling was applied as necessary to keep the temperature below 25°. After addition of the ketone was complete, the mixture was heated to 60–70° for 15 min. It was then cooled and the liquid decanted off. The gummy precipitate was worked three more times with hot benzene. The combined benzene layers were distilled to give 15.1 g (81%) of product. GLC analysis revealed this to be mainly **12** containing a small amount (ca. 5%) of unreacted triethyl phosphonoacetate which could not be removed by simple distillation. The product was therefore used in the next step without further purification. A pure sample was obtained by preparative GLC. For **12**: bp 88–90° (0.20 mm); ir (CCl_4) 2980, 2900, 1715, 1650, 1430, 1378, 1309, 1271, 1249, 1203, 1165 (broad), 1130, 1040, 862 cm^{-1}; ^1H NMR (CCl_3D) δ 1.26 (t, J = 7 Hz, 3), 2.40–2.90 (m, 6), 3.10–3.35 (m, 2), 4.12 (q, J = 7 Hz, 2), 5.66 (broad s, 1); mass spectrum (70 eV) *m/e* (rel intensity) 186 (68, M^+), 157 (24), 141 (38), 139 (11), 125 (12), 114 (10), 113 (100), 112 (81), 111 (23), 99 (14), 97 (21), 85 (16), 79 (39), 77 (12), 67 (15), 55 (11), 47 (10), 45 (16), 41 (17).

Pyrazolidin-3-one-5-spiro[4′-thiacyclohexane] (13a). Compound **13a** was prepared in 92% yield in a manner similar to that described for **1a**. For **13**: mp 137.5–138.5°; ir (CCl_3H) 3430, 3235 (broad), 2905, 2835, 1701 (broad), 1378, 1270, 972, 860 cm^{-1}; ^1H NMR (CCl_3D) δ 1.85–2.10 (m, 4), 2.30 (s, 2), 2.35–2.65 (m, 2), 2.70–3.05 (m, 2); ^{13}C NMR (CCl_3D) δ 24.65 (t), 36.22 (t), 43.98 (t), 61.14 (t), 177.02 (s); mass spectrum (70 eV) *m/e* (rel intensity) 172 (6, M^+), 156 (2), 144 (3), 139 (4), 114 (100), 100 (75), 87 (78), 86 (30), 82 (17), 80 (28), 68 (27), 67 (45), 65 (15), 57 (18), 53 (23), 45 (24), 44 (48), 41 (30).

Anal. Calcd for $C_7H_{12}N_2O$ S: C, 48.81; H, 7.02; N, 16.26. Found: C, 48.64; H, 7.06; N, 15.97.

1-(2,2,2-Trichloroethoxycarbonyl)pyrazolidin-3-one-5-spiro[4′-thiacyclohexane] (13b). Compound **13b** was prepared in 31% yield in a manner similar to that described for **1b**. For **13b**: mp 225–226° dec; ir (CCl_3H) 3410, 2910, 1711 (broad), 1385, 1342, 1312, 1280, 1135 cm^{-1}; ^1H NMR (CCl_3D) δ 2.00–2.30 (m, 2), 2.50–2.90 (m, 6), 2.72 (s, 2), 4.85 (s, 2); mass spectrum (70 eV) *m/e* (rel intensity) no parent, 254 (4), 196 (2, 3-Cl), 154 (12), 114 (90), 111 (24), 99 (90), 98 (47), 96 (53), 86 (88), 85 (41), 81 (34), 79 (46), 68 (36), 67 (67), 65 (24), 63 (33), 61 (100), 60 (28), 53 (40), 47 (32), 45 (50), 44 (57), 43 (36), 41 (60).

Anal. Calcd for $C_{10}H_{13}N_2O_3Cl_3S$: C, 34.55; H, 3.77; N, 8.06. Found: C, 34.39; H, 3.71; N, 7.97.

2-Acetyl-1-(2,2,2-trichloroethoxycarbonyl)pyrazolidin-3-one-5-spiro[4′-thiacyclohexane] (13c) via 3-Acetoxy-1-(2,2,2-trichloroethoxycarbonyl)-2-pyrazoline-5-spiro[4′-thiacyclohexane] (14). Compound **13c** was prepared in 44% yield via compound **14** in a manner similar to that described for **1c** and **3**. For **14**: ^1H NMR (CCl_3D) δ 1.95–2.20 (m, 2), 2.24 (s, 3), 2.55–2.90 (m, 6), 3.10 (s, 2), 4.88 (s, 2). For **13c**: mp 97–99°; ir (CCl_3H) 2910, 1745 (broad), 1375, 1320, 1280, 1123, 1035 cm^{-1}; ^1H NMR (CCl_3D) δ 1.85–2.20 (m, 2), 2.35–3.10 (m, 6), 2.52 (s, 3), 2.74 (s, 2), 4.81 (s, 2); mass spectrum (70 eV) *m/e* (rel intensity) no parent, 142 (8), 114 (18), 100 (19), 99 (14), 96 (10), 86 (17), 85 (17), 67 (10), 61 (12), 60 (96), 59 (12), 45 (93), 44 (79), 43 (100), 42 (19), 41 (31).

Anal. Calcd for $C_{12}H_{15}N_2O_4Cl_3S$: C, 36.99; H, 3.88; N, 7.19. Found: C, 37.03; H, 3.85; N, 6.96.

2-Acetylpyrazolidin-3-one-5-spiro[4′-thiacyclohexane] (13d). Compound **13d** was prepared in 43% yield in a manner similar to that described for **1d**. For **13d**: mp 100.5–101.5°; ir (CCl_3H) 3255, 2905, 2835, 1747, 1699, 1407, 1370, 1275, 972 cm^{-1}; ^1H NMR (CCl_3D) δ 1.85–2.10 (m, 4), 2.30–2.68 (m, 2), 2.45 (s, 3), 2.61 (s, 2), 2.70–3.05 (m, 2), 4.96 (broad s, 1, NH); ^{13}C NMR (CCl_3D) δ 23.91 (q), 24.76 (t), 36.42 (t), 45.86 (t), 56.34 (s), 167.00 (s), 171.91 (s); mass spectrum (70 eV) *m/e* (rel intensity) 214 (24, M^+), 173 (8), 172 (89), 195 (100), 116 (8), 112 (8), 111 (74), 100 (13), 99 (16), 98 (53), 97 (17), 86 (7), 85 (13), 60 (18), 45 (24), 43 (63), 41 (20); uv (EtOH) 226 nm (ϵ 4140), 246 (2500).

Anal. Calcd for $C_9H_{14}N_2O_2S$: C, 50.45; H, 6.59; N, 13.07. Found: C, 50.34; H, 6.49; N, 13.01.

1-Acetamidoazetidin-2-one-4-spiro[4′-thiacyclohexane] (15). Compound **15** was prepared in 45% yield in a manner similar to that described for **5**. For **15**: mp 151–154°; ir (CCl_3H) 3390, 3240 (broad), 2910, 1770, 1705, 1368, 1270, 1085, 965 cm^{-1}; ^1H NMR (CCl_3D) δ 2.00 (s, 3), 2.09 (t, J = 5 Hz, 4), 2.62 (s, 2), 2.70 (t, J = 5 Hz, 4), 8.64 (s, 1, NH); ^{13}C NMR (CCl_3D) δ 20.63 (q), 26.92 (t), 33.91 (t), 45.03 (t), 64.54 (s), 168.30 (s), 170.81 (s); mass spectrum (70 eV) *m/e* (rel intensity) 214 (22, M^+), 196 (11), 172 (76), 144 (71), 114 (77), 112 (65), 111 (62), 99 (82), 98 (56), 86 (59), 67 (45), 43 (100), 41 (42).

Anal. Calcd for $C_9H_{14}N_2O_2S$: C, 50.45; H, 6.59; N, 13.07. Found: C, 50.22; H, 6.58; N, 13.06.

2-Acetyl-1-(2,2,2-trichloroethoxycarbonyl)pyrazolidin-3-one-5-spiro[4′-thiacyclohexane] 4′-Oxide (17). To a solution of 2-acetyl-1-(2,2,2-trichloroethoxycarbonyl)pyrazolidin-3-one-5-spiro[4′-thiacyclohexane] (**13c**, 1.00 g, 2.58 mmol) in methylene chloride (25 ml) cooled to 0° under a nitrogen atmosphere was added dropwise *m*-chloroperoxybenzoic acid (0.44 g, 2.58 mmol) in methylene chloride (5 ml). After stirring at 0° for 12 hr the mixture was allowed to warm to room temperature, after which it was washed three times with 15-ml portions of saturated aqueous sodium bicarbonate. The methylene chloride was dried over $MgSO_4$ and evaporated to give an oil. Column chromatography of the oil on silicic acid using Et_2O–EtOH (90:10 mixture by volume) gave 0.41 g (39%) of a colorless oil which was shown to be **17**: ir (CCl_3H) 2925, 1742 (broad), 1375, 1325, 1290, 1120, 1022 cm^{-1}; ^1H NMR (CCl_3D) δ 1.90–2.35 (m, 2), 2.40–3.30 (m, 6), 2.55 (s, 3), 2.72 (broad s, 2).

Anal. Calcd for $C_{12}H_{15}N_2O_5Cl_3S$: C, 35.53; H, 3.73; N, 6.91. Found: C, 35.65; H, 3.71; N, 7.05.

Reaction of 2-Acetyl-1-(2,2,2-trichloroethoxycarbonyl)pyrazolidin-3-one-5-spiro[4′-thiacyclohexane] 4′-Oxide (17) with Acetic Anhydride. A solution of 2-acetyl-1-(2,2,2-trichloroethoxycarbonyl)pyrazolidin-3-one-5-spiro[4′-thiacyclohexane] 4′-oxide (**17**, 0.085 g, 0.208 mmol) in acetic anhydride (5 ml) was heated at 120° for 2 hr under a nitrogen atmosphere. Immediately after removing the oil bath, aspirator vacuum was applied to the reaction vessel to remove the acetic anhydride solvent. When the reaction vessel had cooled to room temperature, it was placed under high vacuum for a short period of time. ^1H NMR analysis of the crude product resulted in a spectrum which contained major signals for two olefin protons, a doublet at δ 5.64 (J = 10 Hz) and a doublet at 6.56 (J = 10 Hz), along with the other signals expected for **17**. Attempts to purify the sample by column chromatography on silicic acid or by recrystallization resulted in samples in which the olefin signals were either greatly reduced or absent.

2,2-Dimethyl-3-thiacyclopentan-1-one (21). To a solution of NaOH (62 g) in a mixture of water (400 ml) and EtOH (250 ml) at room temperature under a nitrogen atmosphere was added all at once 2-mercaptopropionic acid (82 g, 0.77 mol). After the solution

had cooled to room temperature ethyl 2-bromoisobutyrate (150 g, 0.77 mol) was added all at once. The resulting solution was stirred at room temperature for 5 hr, after which it was cooled in an ice bath and aqueous 12 *N* HCl (100 ml) was added. The resulting acidic solution was extracted with Et_2O which was dried over anhydrous $MgSO_4$ and distilled up to 80°. To the residue was added EtOH (1500 ml) and the mixture refluxed overnight. To the still warm reaction mixture was added Na_2CO_3 (25 g) after which the EtOH was distilled off. To the residue cooled in an ice bath was added aqueous 2 *N* NaOH (100 ml). The basic solution was extracted with Et_2O which was dried over anhydrous $MgSO_4$ and distilled to give 153 g (81%) of the sulfide of α-isobutyric acid β-propionic acid diethyl ester: bp 160° (30 mm); mass spectrum (70 eV) *m/e* 248 (M^+). The sulfide (153 g, 0.62 mol) in Et_2O (350 ml) was dripped slowly into a suspension of NaOEt (84 g, 1.24 mol) in Et_2O (1250 ml) heated at 50°. During the addition the mixture became almost clear and then turned cloudy. The mixture was heated at 50° overnight, after which most of the Et_2O was distilled off. The residue was poured into ice-cold water (200 ml) and aqueous 12 *N* HCl was added slowly until the pH of the solution was strongly acidic. The acidic solution was extracted with Et_2O which was dried over anhydrous $MgSO_4$ and distilled to give 81 g (65%) of foul-smelling 5-ethoxycarbonyl-2,2-dimethyl-3-thiacyclopentan-1-one: bp 71° (0.5 mm); mass spectrum (70 eV) *m/e* 202 (M^+).

The β-keto ester (30 g, 0.148 mol) in a mixture of water (225 ml) and sulfuric acid (25 ml) was refluxed for 4 hr. The cooled solution was saturated with NaCl and extracted with Et_2O. The combined Et_2O was washed with aqueous Na_2CO_3 and then dried over anhydrous $MgSO_4$ and distilled to give 13.94 g (72%) of pure **21**: bp 80° (20 mm); ir (CCl_4) 2970, 1740, 1460, 1405, 1381, 1364, 1275, 1140, 1060, cm^{-1}; ^1H NMR (CCl_3D) δ 1.36 (s, 6), 2.56–2.80 (m, 2), 2.84–3.08 (m, 2); mass spectrum (70 eV) *m/e* (rel intensity) 130 (63, M^+), 112 (72), 75 (7), 74 (100), 59 (65), 45 (8), 41 (12).

An analysis was obtained on the *p*-toluenesulfonic acid hydrazone of ketone **21**, mp 157–159°.

Anal. Calcd for $C_{13}H_{18}N_2O_2S_2$: C, 52.32; H, 6.08; N, 9.39. Found: C, 52.22; H, 6.01; N, 9.26.

Ethyl 2′,2′-Dimethyl-3′-thiacyclopentylideneacetate (20) and Ethyl 5′,5′-Dimethyl-4′-thia-1′-cyclopenten-1′-ylacetate (22). A Wittig reaction on 2,2-dimethyl-3-thiacyclopentan-1-one (**21**) in a manner similar to that used to prepare compound **12** resulted in a 76% yield of distilled product. ^1H NMR analysis revealed this to be a mixture of approximately 60% **20** and 40% **22**. Spectral data were obtained on GLC collected samples of the two esters. For **20**: ir (CCl_3H) 1707 cm^{-1}; ^1H NMR (CCl_3H) δ 1.28 (t, J = 8 Hz, 3), 1.50 (s, 3), 2.95 (t, J = 7 Hz, 2), 3.40 (doublet of triplet, J = 4 and 7 Hz, 2), 4.18 (q, J = 8 Hz), 5.70 (t, J = 4 Hz, 1); mass spectrum (70 eV) *m/e* (rel intensity) 200 (41, M^+), 185 (72), 155 (14), 139 (46), 127 (100), 111 (53), 93 (23), 77 (26). For **22**: ir (CCl_3H) 1731 cm^{-1}; ^1H NMR (CCl_3H) δ 1.28 (t, J = 8 Hz, 3), 1.48 (s, 3), 3.00–3.10 (m, 1), 3.62–3.72 (m, 1), 4.18 (q, J = 8 Hz, 2), 5.63–5.75 (m, 1); mass spectrum (70 eV) *m/e* (rel intensity) 200 (46, M^+), 185 (100), 139 (44), 127 (21), 113 (26), 112 (25), 111 (79), 97 (19), 77 (18), 41 (31).

***cis*-Indazolidin-3-one (26a), *trans*-Indazolidin-3-one (26b), and Cyclohex-1-enecarboxylic Acid Hydrazide (27).** 1-Carboethoxycyclohex-1-ene[18] (**24**) was treated with hydrazine in a manner similar to that described for the preparation of **1a**. Column chromatography of the crude product on silicic acid resulted in the isolation of 0.70 g (5%) of a white solid which was identified as cyclohex-1-enecarboxylic acid hydrazide (**27**) by comparison to a sample prepared below and 0.98 g (7%) of an oil which was identified to be a 90:10 mixture of **26a–26b**: ir (CCl_3H) 3425, 2930, 2860, 1705, 902 cm^{-1}; ^1H NMR (CCl_3D) δ 1.00–2.40 (m, 8), 2.48–2.78 (m, 1, one of **26a** bridgehead proton absorptions), 3.40–3.72 (m, 1, one of **26a** bridgehead proton absorptions), 6.60 (broad s, 2, NH). Trace multiplet absorptions at δ 2.20 and 2.98 were assigned as the two bridgehead protons of **26b**; ^{13}C NMR (CCl_3D) absorptions at δ 42.0 (d) and 58.0 (d) were assigned to **26a** while absorptions at δ 49.0 (d) and 56.5 (d) were assigned to **26b**. The relative intensities of the **26a** to **26b** signals were approximately 9:1; mass spectrum (70 eV) *m/e* (rel intensity) 140 (100, M^+), 125 (16), 109 (71), 98 (67), 97 (43), 81 (67), 71 (24), 67 (32), 54 (22), 41 (22).

The best yields of acylated **26** were obtained by taking the crude reaction mixture and pouring it into ice-cold 2 *N* HCl (90 ml). After washing with Et_2O the acidic aqueous layer was poured into ice-cold 2 *N* K_2CO_3 (100 ml). The basic solution was extracted with CCl_3H which was dried over K_2CO_3 and stripped to leave an oil. The Et_2O soluble (approximately 100 ml Et_2O) portion of this oil was used in the acylation reaction.

Cyclohex-1-enecarboxylic Acid Hydrazide (27). To cyclohex-1-enecarboxylic acid (2.7 g, 0.021 mol) in methylene chloride (50 ml) was added 1.50 g (0.011 mol) of anhydrous K_2CO_3. This mixture was stirred until no gas evolution (CO_2) was observed (ca. 12 hr), at which time it was cooled to 0° and ethyl chloroformate (2.5 g, 0.23 mol) in chloroform (10 ml) containing 1% pyridine was added dropwise. After the mixture was allowed to stir for several hours at 0°, it was poured into a solution of 95% hydrazine (1.0 g, 0.03 mol) in methylene chloride (50 ml) and allowed to stir for another 12 hr. Acid–base work-up gave 1.8 g (60%) of hydrazide **27** as a white solid: mp 78–79° (Bz); ir ($CHCl_3$) 3480, 3340, 2930, 1670, 1625, 1475, 960, and 910 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.61 (m, 4), 2.2 (m, 4), 4.08 (broad s, 2, absent D_2O, NNH_2), 6.70 (broad s, 1, C=CH), and 7.9 (broad s, 1, absent D_2O, $CONHNH_2$); mass spectrum (70 eV) *m/e* (rel intensity) 140 (12, M^+), 125 (3), 109 (100), 81 (73), 79 (29), 77 (8), 53 (25).

Anal. Calcd for $C_7H_{12}N_2O$: C, 59.97; H, 8.63. Found: C, 59.82; H, 8.87.

1-(2,2,2-Trichloroethoxycarbonyl)-*cis*-indazolidin-3-one (28a). A partially purified 90:10 mixture of *cis*- and *trans*-indazolidin-3-one (**26a–26b**) was acylated in a manner similar to that described for the acylation of **1a** to give **1b**. Column chromatography of the crude product on silicic acid resulted in the isolation of 0.65 g (13%) of a white solid which was identified as **28a**: mp 173.5–175.5°; ir (CCl_3H) 3415, 2940, 2860, 1710 (broad), 1450, 1380, 1325, 1125, 905 cm^{-1}; ^1H NMR (CCl_3D) δ 1.00–2.40 (m, 8), 2.88–3.12 (m, 1), 4.44–4.80 (m, 1), 4.87 (s, 2), 9.60 (broad s, 1); ^{13}C NMR (CCl_3D) δ 21.84 (t), 21.92 (t), 22.33 (t), 27.35 (t), 41.19 (d), 58.27 (d), 75.26 (t), 95.03 (s), 151.83 (s), 173.01 (s); mass spectrum (70 eV) *m/e* (rel intensity) 314 (12, 3-Cl, M^+), 272 (8, 3-Cl), 184 (11), 167 (13), 139 (99), 131 (46, 3-Cl), 109 (60), 81 (79), 67 (82), 44 (100), 41 (60).

Anal. Calcd for $C_{10}H_{13}N_2O_3Cl_3$: C, 38.06; H, 4.15; N, 8.88. Found: C, 37.95; H, 4.13; N, 8.88.

1-(2,2,2-Trichloroethoxycarbonyl)-5-methylpyrazolidin-3-one (29). Compound **29** was prepared in 57% yield from 5-methylpyrazolidin-3-one[24] in a manner similar to that described for **1b**. For **29**: mp 165.5–166.5°; ir (CCl_3H) 3410, 2940, 1720 (broad), 1382, 1332, 1080 cm^{-1}; ^1H NMR (CCl_3D) δ 1.45 (d, J = 7 Hz, 3), 2.29 (doublet of doublets, J = 17 and 3 Hz, 1), 3.07 (doublet of doublets, J = 17 and 9.5 Hz, 1) 4.45–4.75 (m, 1), 4.80 (s, 2), 9.10 (broad s, 1, NH); mass spectrum (70 eV) *m/e* (rel intensity) 274 (3-Cl, 3, M^+), 240 (3-Cl, trace), 131 (3-Cl, 8), 100 (32), 97 (20), 69 (27), 61 (36), 44 (100), 42 (47), 41 (55).

Anal. Calcd for $C_7H_9N_2O_3Cl_3$: C, 30.52; H, 3.29; N, 10.17. Found: C, 30.37; H, 3.17; N, 10.15.

2-Acetyl-1-(2,2,2-trichloroethoxycarbonyl)-*cis*-indazolidin-3-one (31a). 1-(2,2,2-Trichloroethoxycarbonyl)-*cis*-indazolidin-3-one (**29**) was acetylated in a manner similar to that described for the acylation of **1b** to give **3**. ^1H NMR analysis of the crude product revealed it to be a 70:30 mixture of the *N*-acetyl derivative **31a** and the *O*-acetyl derivative **32a** as determined by integration of the acetyl methyl singlet absorptions assigned to the two isomers. Heating of the mixture of the two isomers neat under a nitrogen atmosphere at 110° for 3 hr resulted in exclusively the *N*-acetyl isomer. Column chromatography resulted in 0.611 g (58%) of an oil which was identified as **31a**: ^1H NMR (CCl_3D) δ 1.00–1.96 (m, 6), 2.08–2.44 (m, 2), 2.54 (s, 3), 2.92–3.16 (m, 1), 2.56–2.92 (m, 1), 2.82 (AB pattern, J = 12 Hz, 2); ^{13}C NMR (CCl_3D) δ 21.62, 22.50, 23.76, 27.38, 43.29 (d), 58.87 (d), 75.61 (t), 94.75 (s), 154.51 (s), 166.04 (s), 172.64 (s).

Anal. Calcd for $C_{12}H_{15}N_2O_4Cl_3$: C, 40.30; H, 4.23; N, 7.83. Found: C, 40.25; H, 4.15; N, 7.77.

2-Acetyl-*cis*-indazolidin-3-one (33a). Compound **33a** was prepared in 46% yield in a manner similar to **1d**. For **33a**: mp 84–86°; ir (CCl_3H) 2920, 2850, 1748, 1695, 1378, 1286, 1108, 980, 910 cm^{-1}; ^1H NMR (CCl_3D) δ 1.00–2.40 (m, 8), 2.44 (s, 3), 2.80–3.08 (m, 1), 3.48–3.80 (m, 1), 5.52 (broad s, 1, NH); ^{13}C NMR (CCl_3D) δ 22.12, 22.41, 22.82, 23.74, 27.56 (t), 44.65 (d), 53.29 (d), 167.15 (s) 173.21 (s); mass spectrum (70 eV) *m/e* (rel intensity) 182 (5, M^+), 154 (16), 140 (61), 112 (11), 111 (27), 98 (41), 97 (100), 84 (14), 81 (13), 67 (14), 55 (10), 54 (10), 41 (29); uv (EtOH) 227 nm (ϵ 3582), 246 (2885).

Anal. Calcd for $C_9H_{14}N_2O_2$: C, 59.32; H, 7.74; N, 15.37. Found: C, 59.08; H, 7.74; N, 15.38.

1-Acetamido-*cis*-perhydrobenz[*c*]azetidin-2-one (34a). From Irradiation of 33a. Compound **34a** was prepared in a 45% yield in a manner similar to that described for **5**. For **34a**: ir (CCl_3H) 3410, 3230 (broad), 2940, 2860, 1768, 1702, 1450, 1370, 1105 cm^{-1}; ^1H NMR (CCl_3D) δ 1.34–1.98 (m, 8), 1.98 (s, 3), 3.10–3.36 (m, 1), 4.12–4.32 (m, 1), 9.18 (broad s, 1, NH); mass spectrum (70 eV) *m/e* (rel intensity) 182 (5, M^+), 140 (91), 97 (67), 81 (40), 67 (56), 54 (43), 43 (100), 41 (46).

Anal. Calcd for $C_9H_{14}N_2O_2$: C, 59.32; H, 7.74; N, 15.37. Found: C, 59.41; H, 7.87; N, 15.32.

From Acetylation of 36a. 1-Amino-*cis*-perhydrobenz[*c*]azetidin-2-one (**36a**) was acetylated in a manner similar to that described for the acetylation of compound **7** to give **5**. A 90% yield of an oil was isolated which was shown to be **34a** by ir, ^{1}H NMR, and TLC comparison to **34a** obtained from the irradiation of **33a**.

1-Amino-*cis*-perhydrobenz[*c*]azetidin-2-one (36a). To a solution of *cis*-perhydrobenz[*c*]azetidin-2-one (**35a**, 0.69 g, 0.56 mmol) in tetrahydrofuran (which was freshly distilled from lithium aluminum hydride) under a nitrogen atmosphere and cooled to 0° was added over a 10-min period 2.6 *M* BuLi (0.216 ml). The resultant heterogeneous mixture was then stirred for 1 hr at 0°, after which a solution of *O*-mesitylene sulfonylhydroxylamine in tetrahydrofuran (1 ml) was added over a 5-min period. The resultant solution was stirred at 0° for 10 min and then poured in ice-cold aqueous 2 *N* K_2CO_3 (20 ml). The aqueous mixture was extracted with CCl_3H which was dried over K_2CO. Evaporation of the solvent left an oil which was column chromatographed on silicic acid with Et_2O–EtOH (80:20 mixture by volume) eluent. From the column was obtained 11 mg (14%) of an oil which was identified as **36a**: ir (CCl_3H) 2930, 1745 cm^{-1}; ^{1}H NMR (CCl_3D) δ 1.20–2.00 (m, 8), 2.92–3.16 (m, 1), 3.68–3.88 (m, 1), 3.92 (broad s, 2 NH_2); mass spectrum (70 eV) *m/e* (rel intensity) 140 (81, M^+), 109 (22), 108 (46), 82 (37), 81 (100), 67 (80), 54 (47), 41 (41).

Compound **36a** was acetylated to give **34a** for which a correct analysis was obtained (see above, **34a**).

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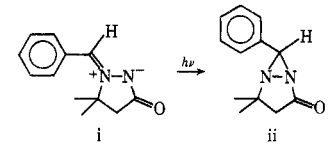
Registry No.—**1a**, 56700-30-2; **1b**, 56700-31-3; **1c**, 56700-32-4; **1d**, 56700-33-5; **2a**, 56700-34-6; **2b**, 56700-35-7; **2c**, 56700-36-8; **2d**, 56700-37-9; **3**, 56700-38-0; **4**, 56700-39-1; **5**, 56700-40-4; **6**, 56700-41-5; **7**, 56700-42-6; **8**, 56700-43-7; **9**, 56700-44-8; **12**, 56700-45-9; **13a**, 56700-46-0; **13b**, 56700-47-1; **13c**, 56700-48-2; **13d**, 56700-49-3; **14**, 56700-50-6; **15**, 56700-51-7; **17**, 56700-52-8; **20**, 56700-53-9; **21**, 52662-41-6; **21** *p*-toluenesulfonic acid hydrazone, 56700-54-0; **22**, 56700-55-1; **24**, 1617-22-7; **26a**, 56700-56-2; **26b**, 56700-57-3; **27**, 56700-58-4; **28a**, 56700-59-5; **29**, 56700-60-8; **31a**, 56700-61-9; **33a**, 56700-62-0; **34a**, 56700-63-1; **35a**, 22031-53-4; **36a**, 56700-64-2; hydrazine, 302-01-2; cyclohexylidene acetate, 1552-91-6; 2,2,2-trichloroethoxycarbonyl chloride, 17341-93-4; 5-methylpyrazolidin-3-one, 10234-76-1; 2-mercaptopropionic acid, 79-42-5; ethyl 2-bromoisobutyrate, 600-00-0; α-isobutyric acid-β-propionic acid diethyl ester sulfide, 52662-42-7; 5-ethoxycarbonyl-2,2-dimethyl-3-thiacyclopentan-1-one, 52704-93-5; cyclohex-1-ene-1-carboxylic acid, 636-82-8.

References and Notes

(1) (a) For Part I see P. Y. Johnson and C. E. Hatch, *J. Org. Chem.*, **40**, 909 (1975). (b) Presented in part at the 169th National Meeting of the American Chemical Society, Philadelphia, Pa., April 9, 1975. (c) Aspects of this work have been reported in preliminary form: P. Y. Johnson, C. E. Hatch, and N. R. Schmuff, *J. Chem. Soc., Chem. Commun.*, 725 (1975).
(2) E. H. Flynn, "Cephalosporins and Penicillins", Academic Press, New York, N.Y., 1972.
(3) (a) J. C. Sheehan and Y. S. Lo, *J. Org. Chem.*, **38**, 3227 (1973); (b) D. M. Brunwin and G. Lowe, *J. Chem. Soc., Chem. Commun.*, 192 (1972).
(4) (a) L. D. Cama and B. G. Christensen, *J. Am. Chem. Soc.*, **96**, 7582 (1974); (b) R. N. Guthikonda, L. D. Cama, and B. G. Christensen, *ibid.*, **96**, 7584 (1974).
(5) Several spiro azetidin-2-ones have been studied as CNS depressants; see M. S. Manhas, J. S. Chib, Y. H. Chiang, and A. K. Bose, *Tetrahedron*, **25**, 4421 (1969).
(6) C. E. Hatch and P. Y. Johnson, *Tetrahedron Lett.*, 2750 (1974).
(7) W. S. Wadsworth and W. D. Emmons, *Org. Synth.*, **45**, 44 (1965).
(8) Prepared analogously to ethyl cyclohexylideneacetate.[7]
(9) Abbreviation for 2,2,2-trichloroethoxycarbonyl chloride. See T. B. Windholtz and D. B. R. Johnson, *Tetrahedron Lett.*, 2555 (1967).
(10) This transformation has been applied to various penicillins which are 3-acylaminoazetidin-2-one derivatives. See W. V. Daehne et al., *J. Med. Chem.*, **13**, 607 (1970).
(11) Precedent for this type of photochemical reaction is found in the photolysis of betaine i to give ii. See M. Schulz and G. West, *J. Prakt. Chem.*, **315**, 711 (1973).



i ii

(12) J. Boutagy and R. Thomas, *Chem. Rev.*, **74**, 87 (1974).
(13) P. Y. Johnson and G. A. Berchtold, *J. Org. Chem.*, **35**, 584 (1970).
(14) P. Y. Johnson, *Tetrahedron Lett.*, 1991 (1972).
(15) For an introduction to the Pummerer reaction see W. E. Parham and L. D. Edwards, *J. Org. Chem.*, **33**, 4150 (1968).
(16) D. E. Wolf and K. Folkers, *Org. React.*, **6**, 410 (1951).
(17) A. H. Cook and R. P. Linstead, *J. Chem. Soc.*, 956 (1934).
(18) S. M. McElvain and R. E. Starn, *J. Am. Chem. Soc.*, **77**, 4571 (1955).
(19) For the procedure used see W. O. Godtfredsen and S. Vangedal, *Acta Chem. Scand.*, **9**, 1498 (1955).
(20) Sulfur nucleophiles have also been shown to add to 1-ethoxycarbonylcyclohex-1-ene to give cis products. See A. Van Bruinsvoort, E. R. De Waard, J. L. Van Bruinsvoort-Meray, and H. O. Huisman, *Recl. Trav. Chim. Pays-Bas*, **92**, 937 (1973).
(21) H. Bestian, H. Biener, K. Clauss, and H. Heyn, *Justus Liebigs Ann. Chem.*, **718**, 94 (1968).
(22) T. Durst and M. J. O'Sullivan, *J. Org. Chem.*, **35**, 2043 (1970).
(23) Y. Tamura, J. Minamikawa, K. Sumoto, S. Fujiiard, and M. Ikeda, *J. Org. Chem.*, **38**, 1239 (1973).
(24) H. Stetter and K. Findeinsen, *Chem. Ber.*, **98**, 3228 (1965).

Aspects of the Chemistry of 1-Aminoazetidin-2-ones and Pyrazolidin-3-ones

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Several reactions of 1-amino-4,4-dimethylazetidin-2-one (**5**) and 1-acetamido-4,4-dimethylazetidin-2-one (**2**) have been examined and their chemistry compared with that of isomeric 5,5-dimethylpyrazolidin-3-ones. The 1-amino β-lactam system was found to undergo ring expansion reactions under a variety of conditions. The irradiation of several 2-alkylpyrazolidin-3-ones to give 1-alkylamino β-lactams in low yields is also discussed.

As part of our work toward the development of approaches to 1-amino- and 1-acylaminoazetidin-2-ones,[1] which we hope to incorporate into total syntheses of penicillin-like systems,[2] we found that these molecules undergo some interesting chemistry, particularly their ring-expansion reactions. While not a well-known class of molecules, 1-aminoazetidin-2-one derivatives have been prepared (1) by photolysis of nitrogen-unsubstituted[1,2] and various 1- or 2-substituted[1,2,3] pyrazolidin-3-ones, (2) by amination of nitrogen unsubstituted azetidin-2-ones,[2,4] (3) by cycloaddition of an acyl hydrazone with ketene,[5] (4) by reaction of an in situ generated 1,1-disubstituted hydrazine with a 3-halo acid chloride,[6] and (5) by an unusual *N*-amino triazole decomposition route.[7]

Results

We have previously reported that 2-acetyl-5,5-dimethylpyrazolidin-3-one (1) undergoes photochemical reaction upon irradiation to give 1-acetamidoazetidin-2-one (**2**) in 65% yield.[1] Since that time, we have found that irradiation