Photochemical Transformations of Small Ring Heterocyclic Compounds. 75. Photochemistry of Arylazirines in Hydroxylic Media[1]

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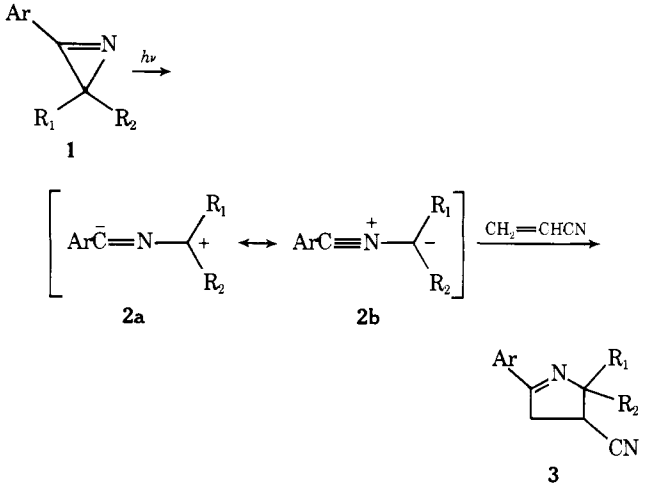
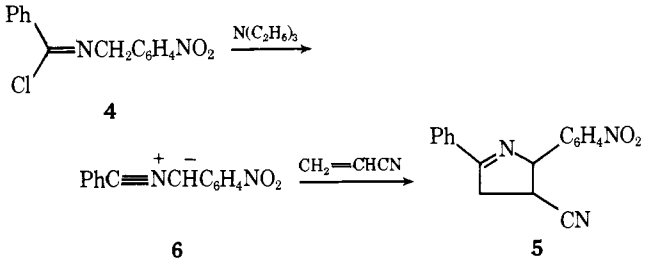
Abstract: Irradiation of substituted arylazirines produces nitrile ylides which react with methanol to give methoxyimines in excellent yield. Deuterium labeling studies indicate that the electron density is highest on the disubstituted carbon atom of the nitrile ylide formed on irradiation. With this conclusion, all of the regiochemical data found in the photoaddition of arylazirines with electron-deficient dipolarophiles can be explained by use of the frontier orbital method. The addition of alcohol to nitrile ylides was also found to occur intramolecularly. A new synthesis of cycloalkanones was devised and is based upon the photolysis of spiroazirines in alcohol followed by aqueous hydrolysis. Irradiation of 2-phenyl-1-azaspiro[2.2]pent-1-ene in methanol however, resulted in a Griffin-type fragmentation and produces ethylene and 2-phenylazirinylidene. This novel carbene reacts with methanol to produce 2-methoxy-2-phenyl-2*H*-azirine (**33**). On further photolysis, azirine **33** undergoes C–C bond cleavage to produce a nitrile ylide which can be trapped by methanol or by an added dipolarophile such as methyl trifluoroacetate. When the irradiation of azaspiro[2.2]pentene is carried out in the presence of oxygen, benzonitrile and carbon monoxide are formed. The formation of these products can best be explained by invoking 2-phenylazirinone as a transient intermediate.

1,3-Dipolar additions of nitrile oxides, nitrile imines, and nitrile ylides are considered to be multicentered cycloaddition processes.[3,4] The independence of solvent polarity,[5] the very negative entropies of activation,[6] and the stereospecificity and regiospecificity[7] point to a highly ordered transition state. In most instances of 1,3-dipolar cycloaddition reactions, when two isomers are possible as a result of the use of unsymmetrical reagents, one isomer usually predominates, often to the exclusion of the alternate isomer.[8,9] The principal question that arises when considering the regioselectivity of 1,3-dipolar additions is whether the two new σ bonds formed on addition of the 1,3-dipolar compound to the dipolarophile are formed simultaneously or sequentially. The mechanism that has emerged from Huisgen's group is that of a single-step, four-center, "no-mechanism" cycloaddition, in which the two new bonds are both partially formed in the transition state, although not necessarily to the same extent.[3,7,10] A symmetry-energy correlation diagram reveals that such a thermal cycloaddition reaction is an allowed process.[7,11,12]

In recent years, the photocycloaddition of arylazirines (**1**) with electron-deficient olefins, leading to Δ^1-pyrroline derivatives **3**, has been extensively studied in these laboratories.[13] The results have been interpreted as proceeding by way of irreversible ring opening of the azirine ring to form a nitrile ylide intermediate **2**. As a 1,3-dipole, this species can be intercepted by a variety of dipolarophiles to form five-membered heterocyclic rings.[14–17] The orientation of the groups in the Δ^1-pyrrolines obtained from the photoaddition process is essentially identical with that observed by Huisgen in related 1,3-dipolar additions.[7,18] For example, treatment of *N*-(*p*-nitrobenzyl)benzimidoyl chloride (**4**) with triethylamine in the presence of acrylonitrile has been found to give Δ^1-pyrroline **5**.[18] This reaction has been interpreted as proceeding via a nitrile ylide intermediate **6**.[19] The experimentally observed regioselectivity of these and other 1,3-dipolar cycloadditions has, until recently, been a most difficult phenomenon to explain. Rationalizations of regioselectivity based on a concerted transition state model have invoked both electronic and steric effects.[3,7,21] A solution to the vexing problem of regioselectivity in 1,3-dipolar cycloadditions has recently been proposed by Houk and coworkers[22–25] who used the frontier orbital method to rationalize the effect of substituents on rates and regioselectivity of 1,3-dipolar cycloadditions.



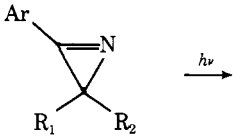


According to the frontier orbital treatment of 1,3-dipolar cycloadditions,[22–26] the relative reactivity of a given 1,3-dipole toward a series of dipolarophiles will be determined primarily by the extent of stabilization afforded the transition state by interaction of the frontier orbitals of the two reactants. When nitrile ylides are used as 1,3-dipoles, the dipole highest occupied (HO) and dipolarophile lowest unoccupied (LU) interaction will be of greatest importance in stabilizing the transition state. The favored cycloadduct will be that formed by union of the atoms with the largest coefficient in the dipole HO and dipolarophile LU. An electron-deficient olefin has the largest coefficient on the unsubstituted carbon in the LU orbital. In order to predict regiose-

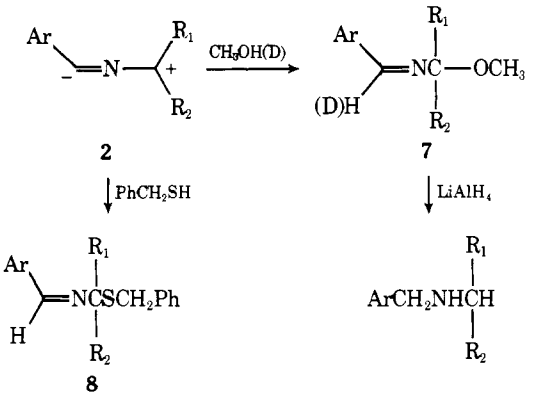
lectivity in the photocycloaddition of arylazirines, it becomes necessary to determine the relative magnitudes of the coefficients in the highest occupied orbital (HO) of the nitrile ylide. To solve this problem, we decided to carry out the irradiation of a number of arylazirines in a hydroxylic medium. In this paper we describe in detail our preliminary observations,[27] along with a study of several hydroxyazirines in which intramolecular addition of the alcohol function to the nitrile ylide can occur. In addition to the mechanistic implications of the above studies, a synthetic application involving the irradiation of several spiroazirines in the presence of methanol is also included.

Results and Discussion

Photolysis of Arylazirines in Protic Solvents. When a solution of 2-phenylazirine (**1a**) in methanol is irradiated through a Pyrex filter, the only product formed (98%) is *N*-methoxymethylbenzalimine (**7a**). Similar irradiation of 2,3-diphenylazirine (**1b**), 2-phenyl-3,3-dimethylazirine (**1c**) and 2-naphthyl-3-methylazirine (**1d**) in methanol afforded analogous photoproducts (**7b–d**) in essentially quantitative yield. Chemical confirmation of structure **7c** was obtained



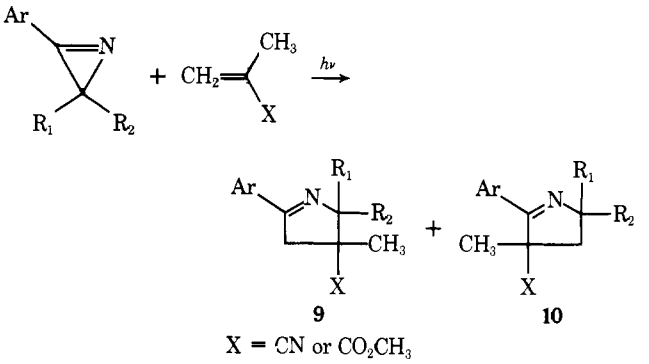
1a, Ar = Ph; $R_1 = R_2 = H$
b, Ar = R_1 = Ph; $R_2 = H$
c, Ar = Ph; $R_1 = R_2 = CH_3$
d, Ar = naphthyl; $R_1 = CH_3$, $R_2 = H$



by acid hydrolysis to benzaldehyde and acetone. Structure **7c** was further confirmed by lithium aluminum hydride reduction to *N*-isopropylbenzylamine. Irradiation of 2,3-diphenylazirine in the presence of benzylmercaptan proceeded similarly and gave adduct **8** in high yield (65%).

The photoconversion of arylazirines (**1**) to methoxyimines **7a–d** and thioimine **8** may be formulated as proceeding via a nitrile ylide intermediate **2a** which undergoes subsequent addition of methanol (or benzylmercaptan). Support for the proposed intermediate **2a** is provided by the deuterium incorporation observed in the course of the photolysis. Irradiation of arylazirines **1** in deuteriomethanol gave deuterated methoxyimines **7a–d**. The extent of deuterium incorporation was determined by mass spectrometry, and the position of deuteration was determined by NMR analysis. The incorporation of a single deuterium atom at the imine carbon is expected for an intermediate corresponding to **2a** in this reaction.

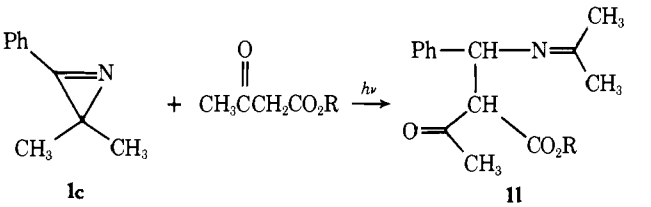
The above results indicate that in the highest occupied orbital of nitrile ylide **2**, the electron density at the disubstituted carbon is greater than at the trisubstituted carbon atom. The preferred regioisomeric transition state will be that in which the larger terminal coefficients of the interacting orbitals are united. Houk has pointed out that with all dipolarophiles except the very electron-rich, nitrile ylide reactions are HO-controlled.[22-25] Reactions of nitrile ylides with electron-rich dipolarophiles have not been observed, indicating that the dipole LU–dipolarophile HO interaction is not very large. The photochemical addition of methanol to the nitrile ylide clearly shows that the larger HO coefficient of the nitrile ylide is, in fact, on the disubstituted carbon atom. With this conclusion, all of the regiochemical data found in the photoaddition of arylazirines[13-17] with dipolarophiles can be explained. Thus, acrylonitrile and methyl acrylate react with various nitrile ylides to give only the 4-substituted regioisomers (i.e., **3** and **5**). Photocycloaddition of arylazirines to α-methylacrylonitrile and methyl methacrylate, on the other hand, give adducts of type **9** and **10** in a 3:2 ratio.[13] The formation of a mixture of cycload-



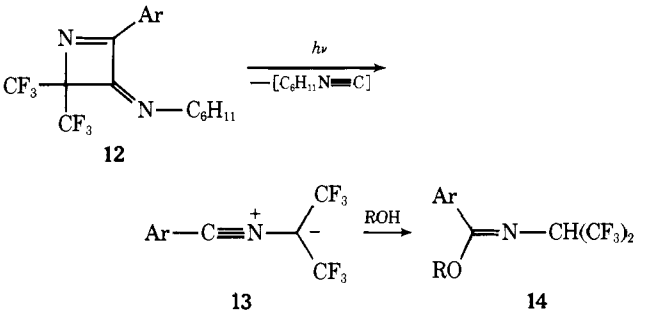
X = CN or CO_2CH_3

ducts in this case can be attributed to the fact that whereas the cyano or ester group enhances the LU coefficient at the unsubstituted carbon atom of the dipolarophile, the methyl group has the opposite effect. The terminal coefficients in the LU of α-methylacrylonitrile and methyl methacrylate are more nearly the same than for the nonmethylated analogues, so that regioselectivity decreases for these dipolarophiles.

It should be noted that Schmid and coworkers[28] have recently reported on the photoaddition of arylazirines with other active hydrogen compounds (e.g., **1c** ($h\nu$) → **11**)

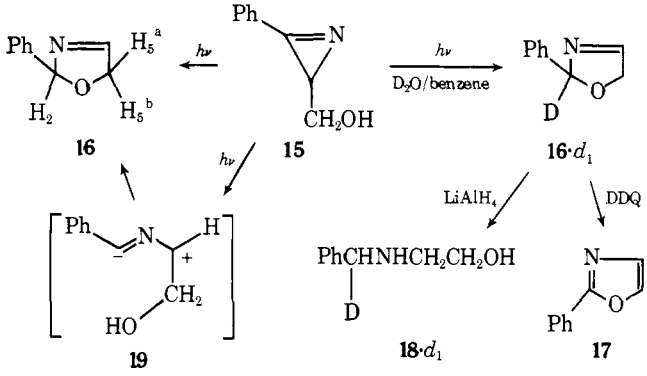


which are complementary to the observations outlined above. A somewhat related case has also been described by Burger who found that irradiation of azetine **12** in an alcohol solvent generated nitrile ylide **13** which could be trapped to give *N*-(hexafluoroisopropyl)benzimidic ester **14**.[29] It is interesting to note that the addition of alcohol to this nitrile ylide occurs in a manner opposite to that encoun-

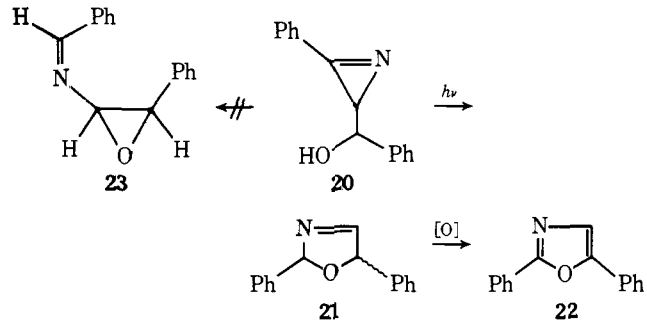


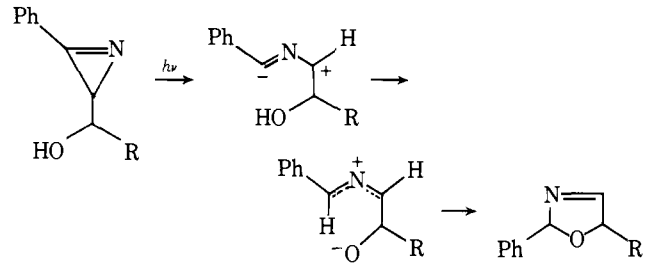
tered in the irradiation of the arylazirines we have examined. The effect of the *gem*-trifluoromethyl groups in Burger's system is apparently such that the coefficient at the trisubstituted carbon atom of the nitrile ylide is now the larger.

Intramolecular Photoadditions of Hydroxyazirines. In the cases reported above, the nitrile ylide intermediate generated from the azirine was trapped by an external alcohol. As a continuation of our investigations in this area, we were particularly interested in determining whether the addition reaction would occur when the alcohol and the azirine ring were constrained to be within the same molecule. In order to probe this possibility, we carried out a study dealing with the photochemistry of a number of hydroxy-substituted azirines. The first compound was 3-phenyl-2*H*-azirine-2-methanol (**15**). This material was readily prepared by the addition of iodine azide to cinnamyl alcohol followed by dehydrohalogenation and thermolysis. Irradiation of **15** in benzene using a 450-W Hanovia immersion apparatus equipped with a Corex filter sleeve led to the complete consumption of reactant in 1.5 h. The sole product isolated (70% isolated yield) was 2-phenyl-3-oxazoline (**16**). The structure of **16** was readily established by examination of its characteristic NMR spectrum ($CDCl_3$, 100 MHz): τ 5.40 (1 H, dd, J = 15.0 and 4.5 Hz), 5.20 (1 H, dd, J = 15.0 and 6.0 Hz), 3.32 (1 H, ddd, J = 6.0, 4.5, and 3.0 Hz), 2.60 (5 H, m), and 2.22 (1 H, d, J = 3.0 Hz). An unusual feature of the NMR spectrum of this compound is the magnitude (4.5–6.0 Hz) of the long-range coupling constant $J_{2,5}$. Although efficient coupling does not normally occur through four σ bonds,[30] the presence of the oxygen atom and possible contributions of the homoallylic type could contribute to the size of $J_{2,5}$.[30,31] Further evidence for the oxazoline structure was obtained by oxidation with DDQ to 2-phenyloxazole (**17**) and by reduction ($LiAlH_4$) to *N*-benzylethanolamine (**18**). The formation of oxazoline **16** may be formulated as proceeding via a nitrile ylide intermediate (**19**) which subsequently transfers a proton from the neighboring hydroxyl group and then collapses to the observed product. Support for the proposed nitrile ylide intermediate was provided by the irradiation of **15** in benzene which had been saturated with D_2O. Mass spectral and nuclear magnetic resonance spectral analysis of the product obtained showed that a single deuterium atom was incorporated at the 2 position of the oxazoline ring, as expected for an intermediate corresponding to **19** in this reaction. The location of the deuterium atom was verified by reduction of **16**-d_1 to *N*-benzylethanolamine-d_1 (**18**-d_1).

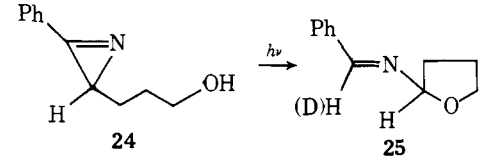


The photolysis of α,3-diphenyl-2*H*-azirine-2-methanol (**20**) proceeded similarly and gave a mixture of *cis*- and *trans*-2,5-diphenyl-3-oxazoline (**21**) (*cis*/*trans* = 3/2) in high yield. The mixture of isomers was cleanly oxidized to 2,5-diphenyloxazole (**22**). It is interesting to note that the irradiation of **20** (and/or **15**) did not afford any of the isomeric *N*-benzylidene epoxide (e.g., **23**). This would suggest that the zwitterion produced on transfer of a proton from the nitrile ylide prefers to collapse to a five-membered rather than a three-membered ring.[32]





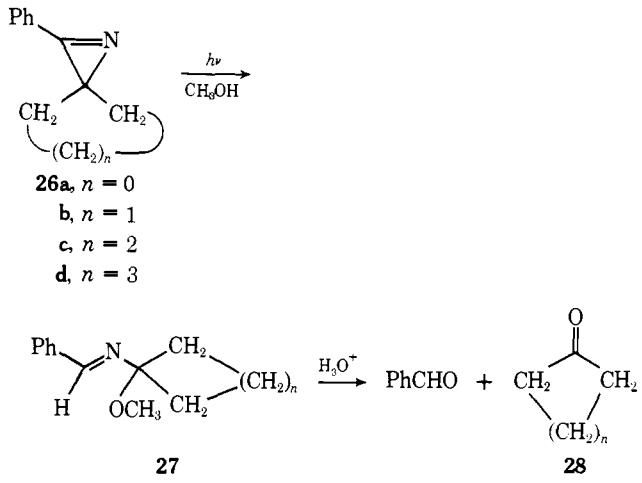
Attention was next turned to the photochemical behavior of 3-phenyl-2*H*-azirine-2-propanol (**24**). This material was formed in high yield from the reaction of iodine azide with 5-phenyl-4-penten-1-ol followed by dehydrohalogenation and thermolysis. Irradiation of **24** in benzene afforded *N*-benzylidenetetrahydro-2-furanamine (**25**) (80%) as the only identifiable product. The structure of **25** is based on its spectral properties (see Experimental Section) and was further substantiated by its ready hydrolysis to benzaldehyde. When the irradiation of **24** was carried out in benzene which had been saturated with D_2O, it was clear that the imine proton had completely exchanged. Again, the formation of **25** can be explained by the internal trapping of a transient nitrile ylide. Photolysis of the hydroxyazirine which contained one less carbon atom (i.e., 3-phenyl-2*H*-azirine-2-ethanol) produced a complex mixture of products and was not pursued further.



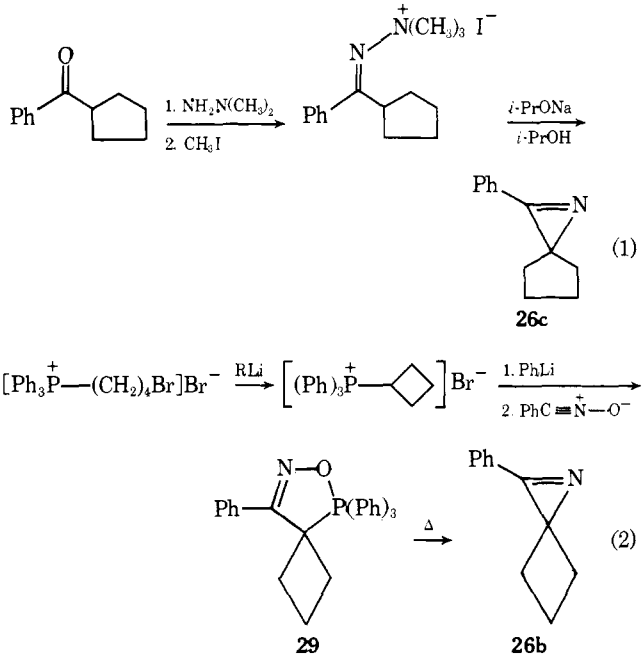
Preparation and Photolysis of Spiroazirines. The results described above suggested to us the possibility of devising a new synthesis of cycloalkanones based upon the photolysis of spiroazirines in methanol followed by aqueous hydrolysis (Scheme I). Therefore, spiroazirines **26a–d** were chosen as model compounds in order to test the feasibility of the proposed sequence.

2-Phenyl-1-azaspiro[5.2]oct-1-ene (**26d**)[33] and 2-phenyl-1-azaspiro[2.2]pent-1-ene (**26a**)[34] were prepared according to literature procedures, while the new azirines, 2-phenyl-1-azaspiro[4.2]hept-1-ene (**26c**) and 2-phenyl-1-azaspiro-[3.2]hex-1-ene (**26b**), were prepared by modifications of these procedures. The formation of **26c** (eq 1) involved treatment of the dimethylhydrazone of cyclopentyl phenyl ketone with methyl iodide followed by reaction with sodium isopropoxide. The synthesis of spiroazirine **26b** (eq 2) required substantial quantities of cyclobutyltriphenylphosphonium bromide. Two procedures have been described for the preparation of cyclobutyltriphenylphosphonium bro-

Scheme I



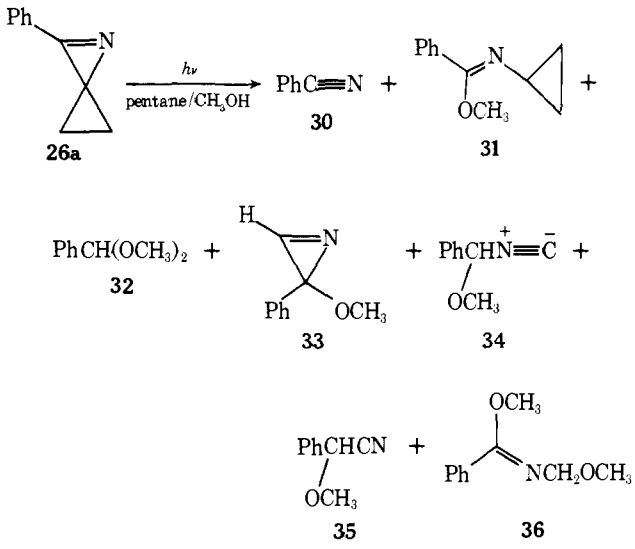
mide from 2-bromobutyltriphenylphosphonium bromide.[35,36] We found both methods to be equally useful, although we prefer the method of Mondon[35] for simplicity and from an economical standpoint. For this reason, and because of the reported[36] inability to repeat Mondon's



work,[35] we report a slight modification with regard to work-up procedure which allows utilization of this method (see Experimental Section). For our purposes, however, the one-step sequence from phosphonium bromide to oxazaphosphole **29** was found to be the preferred route, giving **29** in 45% yield as compared to an overall yield of 37% via the two-step sequence.

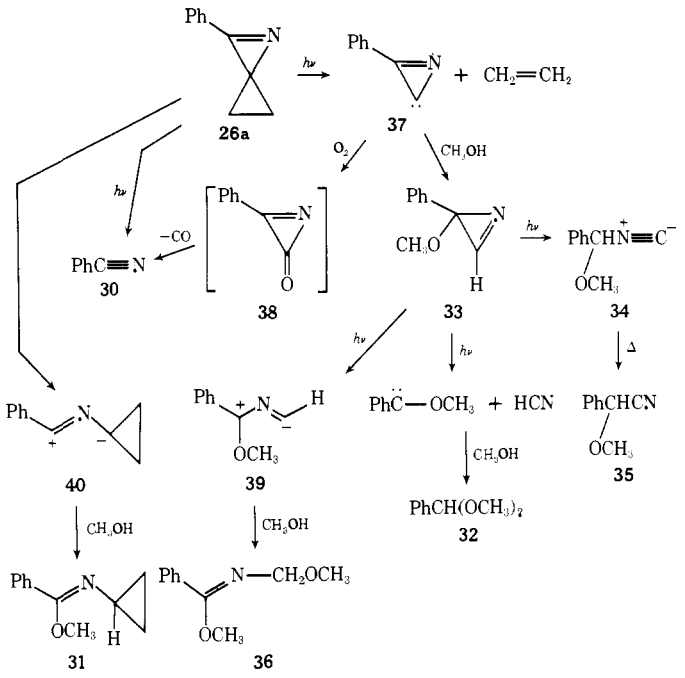
As expected, when a methanol solution of spiroazirine **26d** was irradiated using a 450-W Hanovia immersion well equipped with a Corex filter sleeve, quantitative conversion to methoxyimine **27d** was observed after 1.5 h. Completion of the proposed synthetic sequence was realized by quantitative conversion of **27d** to benzaldehyde and cyclohexanone upon shaking with 10% aqueous hydrochloric acid. Irradiation of spiroazirines **26b** and **26c** in methanol, or in benzene containing excess methanol, also resulted in the formation of imines **27b** and **27c**. Clean conversion to benzaldehyde and the corresponding cycloalkanone **28** was accomplished by treating the photoproduct with a 10% aqueous hydrochloric acid solution. If the methoxyimines derived from azirines **26b** and **26c** were allowed to stand, they would undergo rapid polymerization.

In contrast to the above results, photolysis of 2-phenyl-1-azaspiro[2.2]pent-1-ene (**26a**) under a nitrogen atmosphere in pentane containing excess methanol[37] produced a complex mixture of products. Analysis of the mixture by GLC and NMR indicated the presence of eight major components, seven of which have been identified on the basis of their spectral properties or by comparison with known compounds. Hydrolysis of the crude reaction mixture with 10% aqueous hydrochloric acid produced a mixture of benzaldehyde and methyl benzoate, along with unchanged benzonitrile and methoxynitrile **35**. Examination of the crude photolysis mixture obtained from a short-term irradiation experiment showed the presence of azirine **33** as the major reaction component (NMR ($CDCl_3$): τ 6.72 (3 H, s), 2.97 (5 H, m), and −0.27 (1 H, s)). On further irradiation this compound was isomerized to isonitrile **34** (ir (neat) 2110 cm^{-1}) which was subsequently converted to nitrile **35** on standing in the dark for 12 h.



Three-membered rings are known to undergo [3 → 2 + 1] cycloelimination on irradiation.[38,39] For example, cyclopropane has been photolyzed in the vapor phase and gives methylene and ethylene[40] while photolysis of benzylcyclopropane leads to extensive fragmentation[41] and produces a number of hydrocarbons including ethylene and benzylcarbene. A comprehensive review of the generation of carbenes by photochemical cycloelimination from cyclopropanes has recently appeared.[42] The formation of the major products (see Scheme II) produced from the irradiation of spiroazirine **26a** can also be attributed to an initial photocycloelimination step. This photocycloelimination generates ethylene and the extremely novel carbene, 2-phenylazirinylidene (**37**), which is subsequently trapped by methanol to give azirine **33**. Supporting evidence for this fragmentation was obtained by bubbling the nitrogen purge through a solution of bromine in carbon tetrachloride and trapping ethylene as 1,2-dibromoethane. Benzaldehyde dimethyl acetal (**32**) can be seen as arising by cycloelimination of hydrogen cyanide from azirine **33** followed by reaction of the transient carbene with methanol. Hafner and Bauer[43] had previously reported that the related spiro[2*H*-azirine-2,9′-fluorene] undergoes loss of HCN and generates 9-fluorenylidene, thereby providing good precedent for this suggestion. These workers also reported that the photolysis of spiro[2*H*-azirine-2,9′-fluorene] leads to a mixture of 9-cyano- and 9-isocyanofluorene. This reaction is quite similar to the conver-

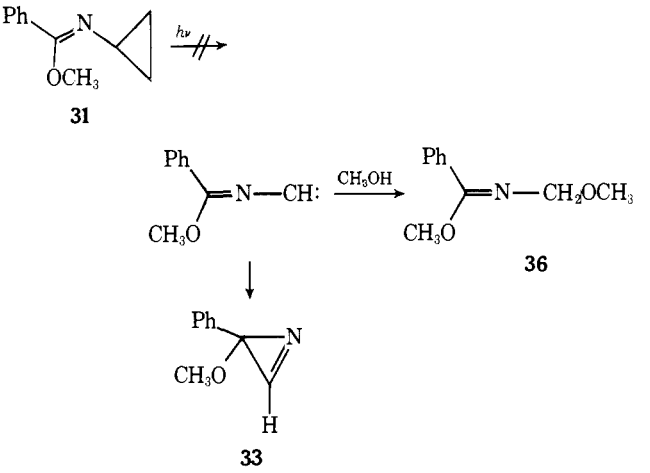
Scheme II.



sion of azirine **33** into isonitrile **34**. Upon extended irradiation, azirine **33** was found to undergo ring opening to generate nitrile ylide **39** which reacts with methanol in the normal fashion to give methoxyimine **36**.

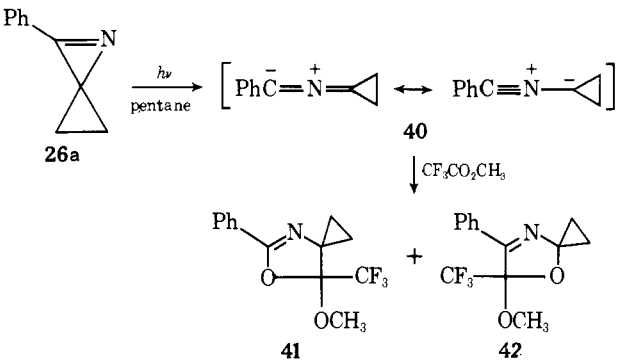
2-Phenylazirinylidene (**37**), by analogy with diphenylcyclopropenylidene,[44] should be a carbene whose normal electrophilicity has been suppressed by conjugation of the double bond electrons of the azirine ring with the vacant p orbital of the carbene. The formation of a spiroadduct is what would be expected from the reaction of a nucleophilic carbene with an electrophilic alkene. Jones and coworkers have shown that both diphenylcyclopropenylidene[44] and cycloheptatrienylidene[45] react with electron-deficient olefins but are inert toward simple alkenes. In an attempt to verify the nucleophilicity of this carbene, we tried to trap **37** with several electron-deficient olefins. Unfortunately, the photolysis of spiroazirine **26a** in the presence of a large excess of dimethyl fumarate or methyl acrylate failed to produce a spiro-cycloadduct derived from the trapping of 2-phenylazirinylidene. However, the irradiation of **26a** in the presence of oxygen met with reasonable success. Trapping of 2-phenylazirinylidene with oxygen would be expected[46] to lead initially to 2-phenylazirinone (**38**). This compound is a considerably interesting molecule since it would represent an example of a heretofore unknown heterocyclic system which could be stabilized by 2π-electron delocalization. It should be noted, however, that although the azirinylium cation has been calculated to have approximately as much stabilization as the cyclopropenylium ion,[47] attempts to prepare the aza system by hydride abstraction from an azirine have so far failed.[48] Also, the opposing dipoles in the azirinone system which are absent in cyclopropenone might be expected to destabilize this three-membered ring. In fact, some recent work by Hassner and Taylor[48] has shown that azirinones are unstable and readily lose carbon monoxide to form nitriles. When the irradiation of spiroazirine **26a** was conducted in pentane in the presence of oxygen, the yield of benzonitrile was significantly increased (ca. 20%). In the absence of oxygen, an extremely small quantity of benzonitrile was formed (<4%) and is presumably derived by competitive cycloelimination from **26a**. Irradiation of the spiroazirine in the presence of excess piperylene under nitrogen produced no significant increase in the amount of benzonitrile (<4%), thus eliminating the possibility that oxygen was acting only as a triplet quencher.[49] The formation of benzonitrile in these experiments can be most reasonably attributed to the trapping of 2-phenylazirinylidene (**37**) with oxygen followed by the loss of carbon monoxide from a thermally unstable azirinone intermediate.

The formation of methyl *N*-cyclopropylbenzimidate (**31**) from the previous irradiation experiments may be formulated as proceeding via a nitrile ylide intermediate (**40**) which undergoes subsequent addition of methanol. It is particularly interesting to note that only a small quantity (ca. 5%) of **31** was obtained from the irradiation of **26a** in methanol. This stands with spiroazirines **26b–d**. From this observation



it would appear as though cycloelimination of ethylene from **26a** is much more efficient than C–C bond scission of the azirine ring. Undoubtedly, the stability of the "aromatic" carbene **37** contributes to this mode of cleavage. Control experiments confirmed that methyl *N*-cyclopropylbenzimidate (**31**) is stable toward irradiation. This observation eliminates a Griffin fragmentation of **31** to an iminocarbene followed by reaction with methanol as the path responsible for the formation of methyl *N*-methoxymethylbenzimidate (**36**) and azirine **33**.

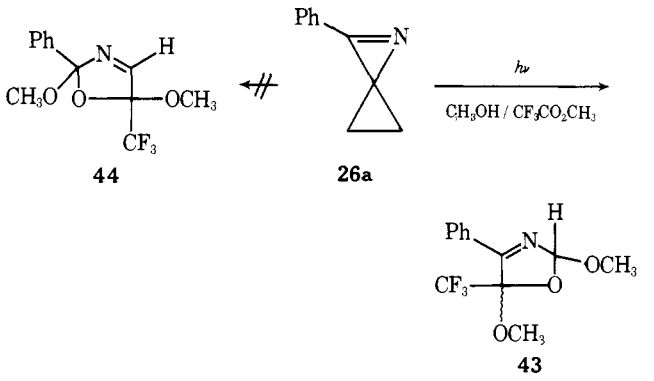
It is also worthwhile to note that the trapping of nitrile ylide **40** with methanol occurs in a different sense from that observed with the other nitrile ylides examined to date. This would imply that the largest HO coefficient of nitrile ylide **40** rests on the cyclopropyl carbon atom. The reluctance to develop a positive charge on the cyclopropyl carbon atom presumably contributes to this reversal in regioselectivity.

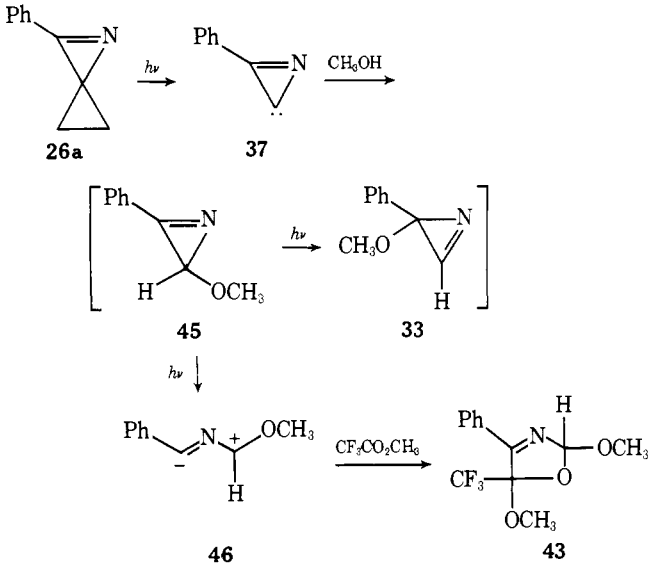


We were able to trap nitrile ylide **40** by carrying out the irradiation of **26a** in pentane in the absence of methanol but in the presence of the very reactive dipolarophile, methyl trifluoroacetate.[50] Two regioisomers **41** (7%) and **42** (2%) were isolated in low yield and were identified by their spectral characteristics (see Experimental Section). The remainder of the reaction mixture consisted of a brownish

polymer, which may stem from the products of a Griffin fragmentation of spiroazirine **26a**. Again, it should be noted that the major cycloadduct obtained corresponds to the trapping of the nitrile ylide (**40**) in the reverse fashion from that normally observed.[50]

A most unusual result was encountered when the irradiation of **26a** was carried out in pentane in the presence of both methanol (1.2 equiv) and methyl trifluoroacetate (excess). Under these conditions, the two stereoisomers of 3-oxazoline **43** (mixture ratio 2.8/1) were the only cycloadducts obtained. If one makes the reasonable assumption that methyl trifluoroacetate, even though it is a reactive dipolarophile, does not participate in bimolecular cycloadditions with unopened azirines, then the chemistry revealed by its presence should be the same as in its absence. Consequently, one might have expected to trap the nitrile ylide (**39**) derived from azirine **33** (i.e., cycloadduct **44**) in the above experiment.[51] The fact that only cycloadduct **43** was obtained suggests that 2-phenylazirinylidene (**37**) reacts with methanol to give mainly azirine **45** which is subsequently converted to nitrile ylide **46** (and thus cycloadduct **43**) on further irradiation. The formation of azirine **33**





could then be explained by a photoinduced methoxy migration of **45** which competes with C–C bond cleavage of the azirine ring. Ciabattoni and Cabell[52] have previously reported that 3-chloro-1-azirines undergo ready isomerization at room temperature via a 2π-electron azacyclopropenyl cation. A similar mechanism would rationalize the apparent photoconversion of azirines **45** and **33** in the above system. It should be noted that 2-phenyl-2-methoxy-2*H*-azirine (**33**) is the only azirine detected in the crude photolysate. An alternate explanation which accounts for the exclusive formation of **33** is that 2-phenylazirinylidene (**37**) reacts with methanol to give both **33** and **45**. Under the photolytic conditions (Corex filter sleeve), the more strongly absorbing 3-phenyl-2-methoxy-2*H*-azirine (**45**) undergoes subsequent secondary photochemistry (e.g., formation of nitrile ylide **46**) and leaves behind the weaker absorbing isomer (i.e., **33**). All attempts to synthesize **45** in order to verify this point have failed. Consequently, at this time we cannot decide which explanation best accounts for the formation of **33**.

Experimental Section[53]

Photoaddition of Methanol to 2-Phenylazirine. A solution of 0.3 g of 2-phenylazirine (**1a**) in 250 ml of absolute methanol was irradiated through a Pyrex filter sleeve for 2.5 h. Removal of the solvent under reduced pressure afforded a nearly colorless oil in quantitative yield whose structure was assigned as *N*-methoxymethylbenzalimine (**7a**) on the basis of the following data: ir (neat) 6.05 μ; uv (95% ethanol) 246, 280, and 285 nm (ϵ 8500, 850, and 750); NMR ($CDCl_3$, 100 MHz) τ 6.60 (3 H, s), 5.00 (2 H, d, J = 2.0 Hz), 2.20–2.60 (5 H, m), and 1.60 (1 H, t, J = 2.0 Hz); *m/e* 149, 134, 119, 105, 91, and 77 (base). Irradiation of 2-phenylazirine in deuteriomethanol afforded deuterated methoxyimine **7a**: NMR ($CDCl_3$) τ 6.60 (3 H, s), 5.00 (2 H, s), and 2.20–2.60 (5 H, m).

Photoaddition of Methanol to 2,3-Diphenylazirine. A solution containing 0.4 g of 2,3-diphenylazirine (**1b**) in 250 ml of anhydrous methanol was irradiated through a Pyrex filter sleeve for 1 h. Removal of the solvent under reduced pressure afforded a light yellow oil in quantitative yield whose structure was assigned as *N*-methoxyphenylmethylbenzalimine (**7b**) on the basis of the following data: ir (neat) 6.05 μ; uv (95% ethanol) 247, 280, and 285 nm (ϵ 15 500, 1600, and 1400); NMR ($CDCl_3$) τ 6.60 (3 H, s), 4.48 (1 H, br s), 2.00–2.80 (10 H, m), and 1.50 (1 H, br s); *m/e* 121 (base), 105, 104, 91, and 77. Irradiation of diphenylazirine **1b** in deuteriomethanol gave deuterated methoxyimine **7b**; NMR ($CDCl_3$) τ 6.60 (3 H, s), 4.48 (1 H, s), and 2.00–2.80 (10 H, m).

Photoaddition of Methanol to 2-Phenyl-3,3-dimethylazirine. A solution containing 0.4 g of 2-phenyl-3,3-dimethylazirine (**1c**) in 250 ml of absolute methanol was irradiated through a Corex filter sleeve for 1.5 h. The solvent was removed under reduced pressure to afford a colorless oil in quantitative yield whose structure was assigned as *N*-methoxydimethylmethylbenzalimine (**7c**) on the basis of the following data: ir (neat) 6.05 μ; uv (95% ethanol) 247, 282, and 285 nm (ϵ 10 200, 100, 80); NMR ($CDCl_3$) τ 8.56 (6 H, s), 6.70 (3 H, s), 2.20–2.60 (5 H, m), and 1.64 (1 H, s); *m/e* 146, 130, 104 (base), 103, 91, and 77.

Chemical confirmation of methoxy imine **7c** was obtained by acid hydrolysis to benzaldehyde and acetone. A solution containing 0.25 g of **7c** in 25 ml of a 10% dioxane–water mixture was treated with 5 drops of concentrated hydrochloric acid at room temperature and was allowed to stand for an additional 15 min. The reaction mixture was diluted with ether, washed with water, and dried over magnesium sulfate. Removal of the solvent under reduced pressure left a colorless oil which was identified as benzaldehyde. The presence of acetone was verified by adding 2,4-dinitrophenylhydrazine to the crude reaction mixture and separating the 2,4-DNPH of acetone.

The structure of methoxy imine **7c** was further confirmed by lithium aluminum hydride reduction to *N*-isopropylbenzylamine. A solution containing 0.31 g of methoxyimine **7c** in 10 ml of ether was added dropwise to a slurry of 0.12 g of lithium aluminum hydride in 50 ml of ether. The mixture was stirred for an additional 30 min before quenching with water and aqueous sodium hydroxide. The salts were filtered and the solvent was removed under reduced pressure to give 0.23 g (89%) of *N*-benzylisopropylamine as a light yellow oil. This material was identical in all respects with an authentic sample.

Photoaddition of Methanol to 3β-Naphthyl-2-methylazirine. A solution containing 0.4 g of 3β-naphthyl-2-methylazirine (**1d**) in 250 ml of absolute methanol was irradiated through a Corex filter sleeve for 1 h. The solvent was removed under reduced pressure leaving a crystalline solid whose structure was assigned as *N*-methoxymethylmethyl-β-naphthalimine (**7d**), mp 87–89 °C; ir (KBr) 6.05 μ; uv (95% ethanol) 224, 244, 248, 275, 283, and 292 nm (ϵ 34 800, 29 000, 35 400, 5100, 7100, and 6480); NMR

($CDCl_3$) τ 8.60 (3 H, d, J = 6.0 Hz), 6.64 (3 H, s), 5.28 (1 H, q, J = 6.0 Hz), and 1.90–2.60 (7 H, m); *m/e* 213, 198, 182, 155, 139, 128, and 59.

Anal. Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09; N, 6.57. Found: C, 78.88; H, 7.06; N, 6.51.

Photoaddition of Benzylmercaptan to 2,3-Diphenylazirine. A solution containing 0.39 g of 2,3-diphenylazirine and 0.25 g of benzylmercaptan in 500 ml of benzene was irradiated through a Pyrex filter sleeve under an argon atmosphere for 1 h. Removal of the solvent under reduced pressure afforded an oil which was recrystallized from 95% ethanol to afford 0.41 g (63%) of a solid, mp 67–69 °C, whose structure was assigned as *N*-thiobenzylphenylmethylbenzalimine (**8**) on the basis of the following data: ir (KBr) 6.05 μ; uv (95% ethanol) 252 nm (ϵ 19 900); NMR ($CDCl_3$) τ 6.32 (2 H, s), 4.44 (1 H, s), 2.00–2.80 (15 H, m), and 1.66 (1 H, s); *m/e* 213, 195, 167, 124, 104, 91, and 77.

Anal. Calcd for $C_{21}H_{19}NS$: C, 79.47; H, 6.03; N, 4.41; S, 10.08. Found: C, 79.39; H, 6.31; N, 4.37; S, 9.83.

Preparation of 3-Phenyl-2*H*-azirine-2-methanol. A solution containing 67 g of cinnamyl alcohol in 25 ml of acetonitrile was added to a rapidly stirred suspension of iodine azide (prepared from 78 g of sodium azide and 30 ml of iodine monochloride) in 450 ml of acetonitrile at 0°. The reaction mixture was allowed to stir at 25° for 6 h and was then poured into 600 ml of water. The aqueous mixture was extracted with ether and the etheral extracts were washed with a 5% aqueous sodium thiosulfate solution followed by water. The ether solution was dried over magnesium sulfate and concentrated under reduced pressure to give a 95% yield of 3-azido-3-phenyl-2-iodo-1-propanol as a pink oil: ir (neat) 2.90 and 4.71 μ; NMR ($CDCl_3$) τ 6.15 (2 H, m), 5.65 (1 H, m), 5.15 (1 H, d, J = 9 0 Hz), and 2.68 (5 H, s).

The above iodo azide was taken up in 1250 ml of ether and was treated with 67.5 g of potassium *tert*-butoxide at 0° for 4 h. The mixture was washed with 800 ml of water, dried over magnesium sulfate, and concentrated under reduced pressure to give 3-azido-3-phenyl-2-propen-1-ol as a yellow oil: ir (neat) 3.00, 4.76, and 6.08 μ; NMR ($CDCl_3$) τ 7.52 (1 H, exchanged with D_2O), 4.98 (2 H, d, J = 7.0 Hz), 2.42 (1 H, t, J = 7.0 Hz), and 2.63 (5 H, s).

The above vinyl azide was taken up in 1 l. of toluene and the solution was heated at reflux for 3 h, at which time the nitrogen evolution had ceased. Removal of the solvent under reduced pressure left a yellow oil which was recrystallized from hexane–ether to give 43 g (63%) of a white solid, mp 58–59 °C, whose structure was assigned as 3-phenyl-2*H*-azirine-2-methanol (**15**) on the basis of the following data: ir (KBr) 2.98 and 5.76 μ; uv (95% ethanol) 245 nm (ϵ 14 000); NMR ($CDCl_3$) τ 7.60 (1 H, m), 7.20 (1 H, br s, exchanged with D_2O), 6.36 (1 H, dd, J = 13.0 and 5.0 Hz), 6.08 (1 H, d, J = 13.0 Hz), 2.60 (3 H, m), and 2.20 (2 H, m); *m/e* 147, 130, 104 (base), and 77.

Anal. Calcd for C_9H_9NO: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.43; H, 6.20; N, 9.44.

Irradiation of 3-Phenyl-2*H*-azirine-2-methanol. A solution containing 300 mg of 3-phenyl-2*H*-azirine-2-methanol in 200 ml of benzene was irradiated through a Corex filter sleeve for 1.5 h. Concentration of the solvent under reduced pressure left a yellow oil which consisted mainly of 2-phenyl-3-oxazoline (**16**) (70%). This material was identified on the basis of its spectral properties: ir (neat) 6.19 μ; NMR ($CDCl_3$) τ 5.40 (1 H, dd, J = 15.0 and 4.5 Hz), 5.20 (1 H, dd, J = 15.0 and 6.0 Hz), 3.32 (1 H, ddd, J = 6.0, 4.5, and 3.0 Hz), 2.60 (5 H, s), and 2.22 (1 H, d, J = 3.0 Hz). Double irradiation of the signal at τ 3.32 caused the collapse of the ABX pattern at τ 5.22 to an AB quartet and the double at τ 2.22 to collapse to a singlet. Double irradiation of the ABX pattern at τ 5.22 collapsed the signal at τ 3.32 to a doublet and did not affect the doublet at τ 2.22. When the irradiation of **15** was carried out in benzene which had been saturated with D_2O, the NMR of the crude photolysate showed an AB quartet at τ 5.22 (2 H, J = 15.0 Hz), a singlet at 2.60 (5 H), and a singlet at 2.22 (1 H). The signal at τ 3.32 had completely disappeared.

Chemical confirmation of structure **16** was obtained by oxidation to 2-phenyloxazole. A solution containing 200 mg of 2-phenyl-3-oxazoline and 700 mg of 2,3-dichloro-5,6-dicyanoquinone (DDQ) in 50 ml of benzene was heated at reflux for 45 min. Removal of the solvent left a dark oil which was chromatographed on a silica gel column using a 75% cyclohexane–ethyl acetate mixture as the eluent. The only fraction obtained was a colorless oil (65%) whose structure was assigned as 2-phenyloxazole (**17**) by comparison with an authentic compound.[54]

The structure of 2-phenyl-3-oxazoline (**16**) was further confirmed by lithium aluminum hydride reduction to *N*-benzylethanolamine. To a solution containing 250 mg of 2-phenyl-3-oxazoline in 50 ml of ether was added 150 mg of lithium aluminum hydride. The reaction was allowed to stir at 25° for 1 h and was then decomposed by the addition of water. The ethereal layer was dried over magnesium sulfate and concentrated under reduced pressure to give *N*-benzylethanolamine (85%). The identity of this product was established by comparison with an authentic sample. The location of the deuterium atom in the sample of 2-phenyl-3-oxazoline obtained from the irradiation of **15** in benzene which had been saturated with D_2O was established by lithium aluminum hydride reduction. The NMR spectrum ($CDCl_3$) showed a triplet at τ 7.35 (2 H, J = 5.0 Hz), a broad singlet at 6.72 (2 H, exchanged with D_2O), a triplet at 6.45 (2 H, J = 5.0 Hz) and a singlet at 6.30 for one benzylic proton.

Preparation of 3-Phenyl-2*H*-azirine-2-propanol. To a suspension of 7.5 ml of iodine monochloride and 22.5 g of sodium azide in 150 ml of acetonitrile was added 10 g of 5-phenyl-4-penten-1-ol[55] at 0°. The reaction mixture was allowed to stir for 4 h at room temperature and was then poured into 200 ml of water and extracted with ether. The ethereal extracts were washed with 5% sodium thiosulfate and water and then dried over magnesium sulfate. Evaporation of the solvent left 15 g of 5-phenyl-4-azido-4-iodopentan-1-ol as a yellow oil: ir (neat) 4.80 μ; NMR ($CDCl_3$) τ 8.20 (4 H, m) 5.59–6.58 (3 H, m), 5.25 (1 H, d, J = 8.0 Hz), and 2.75 (5 H, s). To a solution of 15 g of the above iodo azide in 300 ml of anhydrous ether at −20° was added 23 g of potassium *tert*-butoxide. The reaction mixture was allowed to stir at 0° for 6 h and was then diluted with 200 ml of water. The ethereal solution was washed with water, dried over magnesium sulfate, and evaporated to give 5-phenyl-5-azido-4-penten-1-ol: ir (neat) 4.78 μ; NMR ($CDCl_3$) τ 7.60–8.80 (4 H, m), 6.58 (2 H, t, J = 6.0 Hz), 5.49 (1 H, br s, exchanged with D_2O), 4.71 (1 H, t, J = 7.0 Hz), and 2.78 (5 H, s). A solution of the above vinyl azide in chloroform was heated at reflux for 12 h. Removal of the solvent under reduced pressure left a dark oil which was chromatographed on silica gel with ether to give 1.3 g (12%) of 3-phenyl-2*M*-azirine-2-propanol (**24**) as a colorless oil: ir (neat) 5.79 μ; NMR ($CDCl_3$) 8.28 (4 H, m), 7.71 (1 H, m), 6.60 (1 H, br s, exchanged with D_2O), 6.09–6.40 (2 H, m), and 2.00–2.72 (5 H, m); uv (methanol) 244 nm (ϵ 13 000).

Irradiation of 3-Phenyl-2*H*-azirine-2-propanol. A solution containing 250 mg of 3-phenyl-2*H*-azirine-2-propanol (**24**) in 250 ml of benzene was irradiated using a Corex filter sleeve for 1 h. Removal of the solvent under reduced pressure left a brown oil which was triturated with ether. Evaporation of the ether left a yellow oil (200 mg, 80%) which was assigned the structure of *N*-benzylidenetetrahydro-2-furanamine (**25**) on the basis of its spectral properties: ir (neat) 6.10 μ; NMR ($CDCl_3$) τ 7.6–8.2 (4 H, m), 5.8–6.2 (2 H, m), 4.4–4.60 (1 H, m), 2.19–2.90 (5 H, m), and 1.65 (1 H, d, J = 2.0 Hz); uv (methanol) 247 nm (ϵ 12 000); *m/e* 175 (M^+), 144, 117, 106 (base), 90, and 77. When the irradiation of **24** was carried out in benzene which had been saturated with D_2O the signal at τ 1.65 had completely disappeared. Hydrolysis of the photoproduct with 10% aqueous hydrochloric acid afforded benzaldehyde in good yield (90%).

Preparation of α,3-Diphenyl-2*H*-azirine-2-methanol. To a solution of 14.5 g of 3-phenyl-2-formyl-2*H*-azirine[56] in 500 ml of ether at 0° was added 50 ml of a 2.0 M solution of phenylmagnesium bromide over a 30-min period. The reaction mixture was allowed to stir at room temperature for 4 h and was then quenched by the addition of 250 ml of a saturated ammonium chloride solution. The ethereal solution was washed with water, dried over magnesium sulfate, and concentrated under reduced pressure to give 18.5 g of an orange oil. Chromatography of this material on 300 g of silica gel with 30% ether–pentane gave two diastereomeric alcohols whose structures were assigned as *threo*- (25%) and *erythro*- (32%) α,3-diphenyl-2*H*-azirine-2-methanol (**20**) on the basis of their spectral properties. *threo*-**20** (oil): ir (neat) 3.00 and 5.76 μ; NMR ($CDCl_3$) τ 7.51 (1 H, d, J = 2.0 Hz), 6.96 (1 H, exchanged with D_2O), 5.16 (1 H, d, J = 2.0 Hz), and 2.19–3.00 (10 H, m); *m/e* 223 (M^+), 120, 106, 105 (base), 103, and 77. *erythro*-**20**: mp 106–107 °C; ir (KBr) 3.02 and 5.71 μ; NMR ($CDCl_3$) τ 7.49 (1

H, d, J = 5.0 Hz), 6.22 (1 H, exchanged with D_2O), 5.58 (1 H, d, J = 5.0 Hz), and 2.08–2.83 (10 H, m); uv (95% ethanol) 236 nm (ϵ 13 600); *m/e* 223 (M^+), 120, 106, 105 (base), 103, and 77.

Irradiation of α,3-Diphenyl-2*H*-azirine-2-methanol. A solution containing 300 mg of either the threo or erythro isomer in 550 ml of benzene was irradiated for 3 h using a Pyrex filter sleeve. Removal of the solvent under reduced pressure left a light yellow oil which consisted of a mixture of *cis*- and *trans*-2,5-diphenyl-3-oxazoline **21** (3:2) in 90% yield. The mixture of isomers could not be separated because of the facile hydrolytic decomposition which occurs on chromatography. The trans isomer shows a doublet at τ 4.22 (1 H, J = 5.5 Hz), a doublet of doublets at 3.20 (1 H, J = 5.5 and 2.0 Hz), a multiplet at 2.70 (10 H) and a doublet at 2.30 (1 H, J = 2.0 Hz). The cis isomer shows a doublet at τ 4.38 (1 H, J = 4.5 Hz), a doublet of doublets at 3.40 (J = 4.5 and 2.0 Hz), a multiplet centered at 2.70 (10 H), and a doublet at 2.36 (1 H, J = 2.0 Hz). The mixture of isomers was oxidized by treating 200 mg in 50 ml of benzene with 400 mg of dichlorodicyanoquinone (DDQ) and refluxing the mixture for 30 min. Removal of the solvent left a crude residue which was filtered through a Florisil column with benzene to give 2,5-diphenyloxazole in 85% yield. The 2,5-diphenyloxazole was identified by comparison with an authentic sample.

Preparation of Spiroazirines. 2-Phenyl-1-azaspiro[2.2]pent-1-ene[34] (**26a**) and 2-phenyl-1-azaspiro[2.5]oct-1-ene (**26d**)[33] were prepared according to literature procedures.

2-Phenyl-1-azaspiro[2.3]hex-1-ene. A 15.9-g sample of cyclobutyltriphenylphosphonium bromide, prepared from 4-bromobutyltriphenylphosphonium bromide by either the procedure of Mondon[35] or that of Scherer and Lunt,[36] was placed in 125 ml of anhydrous benzene. The suspension was treated with phenyllithium (45 mmol) and the resulting mixture was stirred for 30 min. To this deep-red solution was added 3.5 g of benzhydroxamoyl chloride in 20 ml of dry benzene over a 1-h period. After completion of the addition, the mixture was stirred for an additional 15 min and was filtered from the phosphonium salts. Removal of the solvent left an orange solid which was triturated with acetone to give 5,5,5,8-tetraphenyl-6-oxa-7-aza-5-phosphaspiro[3.4]oct-7-ene (**29**) (5.0 g, 58%) as a colorless solid: mp 122–123 °C; ir (KBr) 1425, 980, 965, 765, 760, 745, 725, and 700 cm^{-1}; NMR ($CDCl_3$) τ 7.73–8.46 (m, 2 H), 6.93–7.73 (m, 4 H), and 2.24–2.91 (m, 20 H); *m/e* 278 (base), 262, 185, 156, 129, 104, and 103.

Anal. Calcd for $C_{29}H_{26}NOP$: C, 79.98; H, 6.02. Found: C, 80.19; H, 6.07.

Pyrolytic decomposition of the above solid (7.25 g) in a round-bottom flask fitted with a distillation head and dry ice cooled receiver was accomplished by heating in an oil bath at 0.03 mm. Decomposition began at about 110° and heating was continued at 115–129 °C until no more distillate appeared. The distillate consisted of 823 mg (31%) of 2-phenyl-1-azaspiro[2.3]hex-1-ene (**26b**) as a colorless oil: ir (neat) 1730, 1480, 1450, 1240, 1160, 1085, 1070, 960, 885, 765, and 690 cm^{-1}; NMR ($CDCl_3$) τ 6.86–8.30 (m, 6 H), 2.37–2.76 (m, 3 H), and 2.03–2.33 (m, 2 H); *m/e* 157 (M^+), 156 (base), 129, 117, 104, 103, and 77.

2-Phenyl-1-azaspiro[2.4]hept-1-ene. A mixture containing 17.4 g of cyclopentyl phenyl ketone, 12.0 g of *unsym*-dimethylhydrazine, 2.0 g of sodium acetate, and 2 drops of glacial acetic acid was heated in a sealed tube at 120° for 36 h. The reaction mixture was poured into water, extracted with ether, dried over sodium sulfate, and concentrated under reduced pressure. The crude product mixture was distilled to give 18.85 g of a yellow oil: bp 82–86 °C (0.4 mm); ir (neat) 1600, 1490, 1465, 1440, 1025, 980, 775, and 695 cm^{-1}; NMR ($CDCl_3$) τ 8.12–8.62 (m, 8 H), 7.68 and 7.47 (s, 6 H), 7.16 (m, 1 H), and 2.52–2.94 (m, 5 H); *m/e* 216 (M^+), 172, 132, 115, 104 (base), and 103.

A solution containing 16.0 g of the above hydrazone in 40 ml of absolute ethanol was treated with 20.5 g of methyl iodide, and the mixture was gently refluxed for 2 h. The solvent was removed under vacuum to give an orange oil which crystallized on trituration with ether. The solid was recrystallized from acetone to give 17.3 g (75%) of the methiodide salt: mp 133–134 °C; ir (KBr) 1615, 1430, 960, 945, 760, 720, and 705 cm^{-1}.

Anal. Calcd for $C_{15}H_{23}N_2I$: C, 50.29; H, 6.47. Found C, 50.21; H, 6.48.

To a solution of sodium (727 mg) dissolved in 100 ml of dry isopropyl alcohol, maintained at 40°, was added 14.0 g of the above methiodide salt, and the mixture was stirred at 40° for 1 h. The solvent was removed under vacuum and the residual salts were separated by extraction with ether. Removal of the ether and distillation of the residue gave 4.27 g (79%) of 2-phenyl-1-azaspiro[2.4]hept-1-ene (**26c**) as a colorless oil: bp 59–60 °C (0.1 mm): ir (neat) 1740, 1490, 1450, 880, 765, and 690 cm^{-1}; NMR ($CDCl_3$) τ 7.80–8.75 (m, 8 H), 2.42–2.70 (m, 3 H), and 2.15–2.36 (m, 2 H); *m/e* 171 (M^+), 170 (base), 143, 104, and 77.

Irradiation of 2-Phenyl-1-azaspiro[2.5]oct-1-ene (26d). A 300-mg sample of **26d** in 250 ml of dry methanol was irradiated under a nitrogen atmosphere through a Corex filter sleeve for 1.5 h. Removal of the solvent under reduced pressure gave benzal-1-methoxycyclohexylamine (**27d**) as a pale yellow oil in quantitative yield: ir (neat) 1640, 1445, 1155, 1085, 1070, 1050, 940, 755, and 690 cm^{-1}; NMR ($CDCl_3$) τ 8.36 (m, 10 H), 6.82 (s, 3 H), 2.50–2.83 (m, 3 H), 2.15–2.41 (m, 2 H), and 1.77 (s, 1 H). An NMR sample of **27d** was hydrolyzed by addition of 10% aqueous hydrochloric acid. Integration, using 1,1,2,2-tetrachloroethane as an internal standard, indicated quantitative conversion to benzaldehyde and cyclohexanone.

Irradiation of 2-Phenyl-1-azaspiro[2.4]hept-1-ene. A 233-mg sample of 2-phenyl-1-azaspiro[2.4]hept-1-ene (**26c**) in 250 ml of dry benzene to which 2 ml of anhydrous methanol had been added was irradiated through a Corex filter sleeve for 10 min. Removal of the solvent gave 277 mg of a yellow oil which consisted mainly of benzal-1-methoxycyclopentylamine (**27c**): ir (neat) 1670, 1640, and 1445 cm^{-1}; NMR ($CDCl_3$) τ 7.5—8.5 (8 H, m), 6.77 (3 H, s), 2.49–2.80 (3 H, m), 2.18–2.38 (2 H, m), and 1.73 (1 H, s). The crude photolysate was immediately treated with 5 ml of a 10% aqueous hydrochloric acid solution, and the mixture was stirred at room temperature for 30 min. The aqueous layer was withdrawn, and the organic layer was filtered through anhydrous sodium sulfate. Removal of the solvent under reduced pressure gave a mixture of benzaldehyde (75%) and cyclopentanone as indicated by NMR integration.

Irradiation of 2-Phenyl-1-azaspiro[2.3]hex-1-ene. A 265-mg sample of 2-phenyl-1-azaspiro[2.3]hex-1ene (**26b**) in 250 ml of dry methanol was irradiated through a Corex filter sleeve for 30 min. Removal of the solvent under reduced pressure left 315 mg of a yellow oil (99%) consisting largely of benzal-1-methoxycyclobutylamine (**27b**): ir (neat) 1675, 1640, 1490, 1445, 1150, 760, and 695 cm^{-1}; NMR ($CDCl_3$) τ 7.44–8.35 (4 H, m), 6.78 (3 H, s), 2.44–2.87 (3 H, m), 2.06–2.40 (2 H, m), and 1.71 (1 H, s); *m/e* 189 (M^+), 174, 160, 157, 156, 129, 104 (base), and 77. An NMR sample of **27b** was hydrolyzed by addition of 10% aqueous hydrochloric acid. The NMR of the resultant mixture indicated clean conversion to benzaldehyde and cyclobutanone in a 1:1 ratio.

Ground-State Addition of Methanol to 2-Phenyl-1-azaspiro[2.2]-pent-1-ene. A 44-mg sample of 2-phenyl-1-azaspiro[2.2]pent-1-ene (**26a**) in 40 ml of anhydrous methanol was stirred at room temperature for 4 h. Removal of the solvent gave 58 mg (93%) of 1-benzoylcyclopropylamine dimethyl acetal as a colorless oil: NMR ($CDCl_3$) τ 9.38–9.60 (2 H, m), 8.71–9.00 (2 H, m), 8.65 (2 H, br s, D_2O exchangeable), 6.83 (6 H, s), and 2.42–2.87 (5 H, m). In a similar run, 23 mg of **26a** in 25 ml of dry benzene containing 0.2 ml of dry methanol was allowed to stand at room temperature for 4 h. Removal of the solvent gave back unreacted starting material. In analogous control experiments, azirines **26b**, **26c**, and **26d** did not undergo ground-state addition of methanol.

Irradiation of 2-Phenyl-1-azaspiro[2.2]pent-1-ene. (A) **In Benzene.** A solution containing 246 mg of azirine **26a** in 250 ml of dry benzene containing 2 ml of anhydrous methanol was flushed with nitrogen and photolyzed through a Corex filter sleeve for 40 min. Removal of the solvent gave 264 mg of a red-black oil, displaying weak ir absorption at 2220 cm^{-1} and somewhat stronger bands at 2120 and 1670 cm^{-1} and having several methoxy singlets in the NMR. The oil was dissolved in ether and hydrolyzed by addition of a 10% aqueous hydrochloric acid solution. The ethereal layer was dried and concentrated under reduced pressure to give 151 mg of a red-black oil. This was triturated with pentane, filtered, and the solvent removed to give 92 mg of a yellow oil. Analysis by gas chromatography (7 ft column, 10% UCON on Chromosorb W, 150°) showed, in order of elution, benzonitrile, methyl benzoate, and methoxyphenylacetonitrile (**35**). Benzaldehyde, shown to be present by NMR, did not elute from the column.

(B) **In Pentane.** A 219-mg sample of spiroazirine **26a** in 250 ml of pentane containing 2 ml of anhydrous methanol was photolyzed

for 45 min, and the solvent was removed to give 255 mg of an orange oil which slowly turned red on standing. The infrared spectrum of the crude photolysate showed a strong bond at 2120 cm^{-1} The NMR spectrum showed the presence of isonitrile **34** (16%): NMR ($CDCl_3$) τ 4.40 (s, 1 H), and 6.48 (3 H, s). After the mixture was allowed to stand in the dark at room temperature, these signals diminished with a corresponding intensification of the absorptions of methoxyphenylacetonitrile (**35**). Complete conversion was attained overnight, with concomitant disappearance of the 2120-cm^{-1} band in the infrared. Hydrolysis of the reaction mixture with 10% aqueous hydrochloric acid gave similar results to those described above.

An authentic sample of methoxyphenylacetonitrile (**35**) was prepared by treating 1.56 g of α-chloro-α-phenyl dimethyl ether[57] in 10 ml of anhydrous ether with 1.34 g of silver cyanide and allowing the mixture to reflux for 3 h. The mixture was filtered and the filtrate evaporated to afford a quantitative yield of nitrile **35**: ir (neat) 1495, 1455, 1195, 1080, 965, 905, 755, and 695 cm^{-1}; NMR ($CDCl_3$) τ 6.49 (3 H, s), 4.83 (1 H, s), and 2.60 (5 H, s); *m/e* 147 (M^+), 132, 121, 116 (base), 105, 89, and 77.

A 172-mg sample of spiroazirine **26a** was irradiated as above and the nitrogen purge was bubbled through a solution of bromine in carbon tetrachloride. Upon completion of the photolysis, the carbon tetrachloride solution was washed with sodium thiosulfate solution and evaporated to give a yellow oil which consisted of a 1,2-dibromoethane (NMR ($CDCl_3$) τ 6.34) by comparison with an authentic sample. Evaporation of the pentane solution gave 189 mg of a yellow oil. The crude photolysate was analyzed by gas chromatography using propiophenone as an internal standard. Integration provided the following yield data (all materials were identified by comparison with known compounds or were independently synthesized as indicated below): peak 1, benzonitrile (4%); peak 2, benzaldehyde dimethyl acetal (6%); peak 3, methoxyphenylacetonitrile (8%); peak 4, methyl-*N*-cyclopropylbenzimidate (**31**) (5%); peak 5, methyl *N*-methoxymethylbenzimidate (**36**), (14%).

An authentic sample of methyl *N*-cyclopropylbenzimidate (**31**) was prepared by treating 670 mg of *N*-cyclopropylbenzamide with 867 mg of phosphorus pentachloride and heating the mixture gently until hydrogen chloride gas evolution had ceased (ca. 1.5 h). The phosphorus oxychloride was removed under reduced pressure to leave behind *N*-cyclopropylbenzimidoyl chloride as a pale yellow oil: ir (neat) 1655, 1445, 1355, 1235, 1160, 955, 895, 765, and 690 cm^{-1}; NMR ($CDCl_3$) τ 8.79–9.02 (4 H, m), 6.48 (1 H, m), 2.48–2.72 (3 H, m), and 1.91–2.10 (2 H, m); *m/e* 153, 144 (base), 124, 104, 89, and 77. A 580 mg sample of *N*-cyclopropylbenzimidoyl chloride was dissolved in pentane and 180 mg of sodium methoxide was added. The mixture was refluxed for 20 h and filtered; the solvent was removed to afford 535 mg of a pale yellow oil, consisting largely of methyl *N*-cyclopropylbenzimidate (**31**): ir (neat) 1660, 1445, 1280, 1190, 1120, 955, 895, 775, 765, and 700 cm^{-1}; NMR ($CDCl_3$) τ 9.24–9.42 (4 H, m), 7.08–7.32 (1 H, m), 6.27 (3 H, s), and 2.39–2.69 (5 H, m); *m/e* 175 (M^+), 147, 144, 105 (base), 91, and 77.

An authentic sample of methyl *N*-methoxymethylbenzimidate (**36**) was prepared by dissolving 1.71 g of methyl benzimidate hydrochloride and chloromethyl methyl ether (0.8 g) in 100 ml of carbon tetrachloride. To this mixture was added 2.8 ml of triethylamine and the mixture was stirred overnight at room temperature and filtered; the solvent was evaporated to give 1.45 g of a yellow oil. The oil was distilled with gentle warming at 0.03 mm and the distillate was collected with the aid of a dry ice–2-propanol trap. The pot residue (35%) consisted of relatively pure methyl *N*-methoxymethylbenzimidate (**36**): ir (neat) 1670, 1445, 1430, 1275, 1200, 1110, 1075, 1030, 930, 775, and 700 cm^{-1}; NMR ($CDCl_3$) τ 6.60 (3 H, s), 6.12, (3 H, s), 5.22 (2 H, s), and 2.59 (5 H, s); *m/e* 179 (M^+), 164, 148, 134, 119, 105 (base), 103, 91, and 77. Treatment of an NMR sample of **36** with 10% aqueous hydrochloric acid resulted in quantitative conversion to methyl benzoate.

Photolysis of 2-Phenyl-1-azaspiro[2.2]pent-1-ene in the Presence of Oxygen. A 114-mg sample of spiroazirine **26a** was dissolved in 200 ml of pentane and irradiated for 30 min while a constant stream of oxygen was being passed through the system. The solution was filtered through Celite and evaporated to give 67 mg of an orange oil exhibiting a strong 2220-cm^{-1} band in the infrared. Analysis by gas chromatography using propiophenone as an internal standard indicated the yield of benzonitrile to be 16 mg (20%). In another run, spiroazirine **26a** (143 mg) and piperylene (562 mg) under argon produced only 5 mg (4%) of benzonitrile.

Short-Term Irradiation of 2-Phenyl-1-azaspiro[2.2]pent-1-ene in Pentane. A 100-mg sample of spiroazirine **26a** was photolyzed in pentane under the normal conditions for only 5 min. Removal of the solvent and analysis of the crude photolysate by NMR showed that, in addition to starting material, a new product (20% conversion) was formed whose structure was assigned as 2-methoxy-2-phenyl-2*H*-azirine (**33**). After 10 min of irradiation, the NMR spectrum indicated a 1:1 mixture of spiroazirine **26a** and azirine **33**, along with smaller amounts of the previously observed photoproducts. By intermittent monitoring of an NMR sample over a period of 2 days, the absorptions due to 2-methoxy-2-phenyl-2*H*-azirine (**33**) (NMR ($CDCl_3$) τ 6.72 (3 H, s), 2.79 (5, H, m), and −0.27 (1 H, s)) were observed to slowly decrease in intensity and be replaced by broad, indistinct absorptions. In another run, spiroazirine **26a** was irradiated for 15 min, at which time the NMR spectrum showed a substantial increase in the amounts of the final photoproducts with respect to the amount of 2-methoxy-2-phenyl-2*H*-azirine (**33**), with some starting spiroazirine **26a** still being present.

Irradiation of 2-Phenyl-1-azaspiro[2.2]pent-1-ene in the Presence of Methyl Trifluoroacetate. A. A 274-mg sample of spiroazirine **26a** and 13.5 g of methyl trifluoroacetate in 250 ml of anhydrous benzene was irradiated through a Corex filter sleeve for 1 h. The solvent was removed under reduced pressure and the residue was triturated with pentane, filtered, and reevaporated to give 215 mg of a red-orange oil. This material was chromatographed on a thick layer plate using chloroform as the eluent. The first band obtained contained 11 mg (2%) of a yellow oil whose structure was identified as 3-oxazoline (**42**) on the basis of the following data: ir (CCl_4) 1635, 1445, 1320, 1190, and 1080 cm^{-1}; NMR ($CDCl_3$) τ 8.51 (4 H, m), 6.62 (3 H, s), 2.40–2.64 (3 H, m), and 1.90–2.06 (2 H, m); *m/e* 271 (M^+), 256, 240, 229, 202, 174, 91, and 77; uv (methanol) 255 nm (ϵ 9900). The second band isolated from the thick layer plate was identified as cyclopropyl phenyl ketone (12%) by comparison with an authentic sample. The third band contained 37 mg of 2-oxazoline **41** (7%): ir (CCl_4) 1655, 1190, 1135, 1085, 1065, and 1010 cm^{-1}; NMR ($CDCl_3$) τ 8.52–8.84 (4 H, m), 6.55 (3 H, s), 2.40–2.60 (3 H, m) and 1.92–2.10 (2 H, m); *m/e* 271 (M^+), 241, 202, 174, 143, 105, and 77; uv (methanol) 252 nm (ϵ 14 900).

B. A 296-mg sample of spiroazirine **26a** was dissolved in 200 ml of pentane which contained 79 mg of methanol and 13.5 g of methyl fluoroacetate. The mixture was irradiated for 45 min, filtered through Celite to remove precipitated polymer, and evaporated to give 389 mg of a yellow-orange oil. Thick layer chromatography using a 9:1 chloroform–ether mixture as the eluent gave phenyl cyclopropyl ketone and two additional bands. The major band contained 80 mg (14%) of a yellow oil whose structure was assigned as 2,5-dimethoxy-4-phenyl-5-trifluoromethyl-3-oxazoline (**43**): ir (CCl_4) 1640, 1445, 1325, 1195, 1175, and 1000 cm^{-1}; NMR ($CDCl_3$) τ 6.67 (3 H, s), 6.46 (3 H, s), 3.32 (1 H, s), 2.42–2.70 (3 H, m), and 1.86–2.00 (2 H, m); *m/e* 244, 217, 202, 172, 147, 105, 104 (base), and 77; uv (methanol) 252 nm (ϵ 15 600). The minor band could not be completely separated from the major band. On the basis of its NMR (($CDCl_3$) τ 6.60 (3 H, s), 6.35 (3 H, s), 3.63 (1 H, s), 2.40–2.70 (3 H, m), and 1.83–2.08 (2 H, m)), this material (30 mg, 5%) was considered to be a stereoisomer of 2,5-dimethoxy-4-phenyl-5-trifluoromethyl-3-oxazoline.

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References and Notes

(1) For part 74, see A. Padwa and P. H. J. Carlsen, *J. Am. Chem. Soc.*, **98**, 2006 (1976).
(2) National Institutes of Health Postdoctoral Fellow, 1974–1975; Public Health Service Research Grant No. 1-F22-CA-02787-01 from the National Cancer Institute.
(3) For recent reviews see (a) R. Huisgen, *Angew. Chem.*, **75**, 741 (1963); *Angew. Chem., Int. Ed. Engl.*, **2**, 633 (1963); (b) R. Huisgen, R. Grashey, and J. Sauer in "The Chemistry of Alkenes", S. Patai, Ed., Interscience, London, 1964, pp 806–878.

(4) G. L. Abbé, *Chem. Rev.*, **69**, 345 (1969).
(5) R. Huisgen, G. Szeimies, and L. Mobius, *Chem. Ber.*, **100**, 2494 (1967); R. Huisgen, H. Stangl, H. J. Stern, and H. Wagenhofer, *Angew. Chem.*, **73**, 170 (1961).
(6) R. Huisgen, L. Mobius, G. Muller, H. Stangl, G. Szeimies, and J. M. Vernon, *Chem. Ber.*, **98**, 3992 (1965).
(7) R. Huisgen, *J. Org. Chem.*, **33**, 2291 (1968); **41**, 403 (1976).
(8) R. Huisgen, H. Gotthardt, and R. Grashey, *Chem. Ber.*, **101**, 536 (1968).
(9) M. Christl and R. Huisgen, *Tetrahedron Lett.*, 5209 (1968).
(10) An alternative mechanism that has been proposed is a two-step process involving a spin-paired diradical intermediate; see R. A. Firestone, *J. Org. Chem.*, **33**, 2285 (1968); **37**, 2181 (1972); *J. Chem. Soc. A*, 1570 (1970).
(11) A. Eckell, R. Huisgen, R. Sustmann, G. Wallbillich, D. Grashey, and E. Spindler, *Chem. Ber.*, **100**, 2192 (1967).
(12) R. Hoffmann and R. B. Woodward, *Acc. Chem. Res.*, 1, 20 (1968).
(13) A. Padwa and J. Smolanoff, *J. Am. Chem. Soc.*, **93**, 548 (1971); A. Padwa, M. Dharan, J. Smolanoff, and S. I. Wetmore, *ibid.*, **94**, 1395 (1972); **95**, 1945 (1973); *Pure Appl. Chem.*, **33**, 269 (1973); A. Padwa and S. I. Wetmore, *J. Org. Chem.*, **38**, 1333 (1973); **39**, 1396 (1974); *J. Am. Chem. Soc.*, **96**, 2414 (1974); A. Padwa, J. Smolanoff, and A. Tremper, *Tetrahedron Lett.*, 29, 33 (1974).
(14) A. Padwa, D. Dean, and J. Smolanoff, *Tetrahedron Lett.*, 4087 (1972).
(15) N. Gakis, M. Marky, H. J. Hansen, and H. Schmid, *Helv. Chim. Acta*, **55**, 748 (1972).
(16) H. Giezendanner, M. Marky, B. Jackson, H. J. Hansen, and H. Schmid, *Helv. Chim. Acta*, **55**, 745 (1972).
(17) B. Jackson, M. Marky, H. J. Hansen, and H. Schmid, *Helv. Chim. Acta*, **55**, 919 (1972).
(18) R. Huisgen, H. Stangl, H. J. Sturm, and H. Wagenhofer, *Angew. Chem., Int. Ed. Engl.*, 1, 50 (1962); *Chem. Ber.*, **105**, 1258 (1972).
(19) Huisgen has pointed out that the regioselectivity of this reaction is opposite to that expected on the basis of the nitrilium resonance representation **6**;[20] see R. Huisgen, *Angew. Chem., Int. Ed. Engl.*, **2**, 565 (1963).
(20) Huisgen also notes that it is not meaningful to assign an electrophilic and nucleophilic end to a 1,3-dipole: R. Huisgen, *Bull. Soc. Chim. Fr.*, 3431 (1965).
(21) R. Huisgen, R. Sustmann, and K. Bunge, *Chem. Ber.*, **105**, 1324 (1972), and references cited therein.
(22) K. N. Houk, *J. Am. Chem. Soc.*, **94**, 8953 (1972).
(23) K. N. Houk, J. Sims, R. E. Duke, Jr., R. W. Strozier, and J. K. George, *J. Am. Chem. Soc.*, **95**, 7287 (1973).
(24) K. N. Houk, J. Simms, C. R. Watts, and L. J. Luskus, *J. Am. Chem. Soc.*, **95**, 7301 (1973).
(25) J. Sims and K. N. Houk, *J. Am. Chem. Soc.*, **95**, 5798 (1973).
(26) R. Sustmann, *Tetrahedron Lett.*, 2717 (1971).
(27) For a preliminary report see A. Padwa and J. Smolanoff, *J. Chem. Soc., Chem. Commun.*, 342 (1973); A. Padwa and J. Rasmussen, *J. Am. Chem. Soc.*, **97**, 5912 (1975).
(28) P. Claus, P. Gilgin, H. J. Hansen, H. Heimgartner, B. Jackson, and H. Schmid, *Helv. Chim. Acta*, **57**, 2173 (1974).
(29) K. Burger, W. Thenn, and E. Muller, *Angew. Chem., Int. Ed. Engl.*, **12**, 149 (1973).
(30) N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry", Holden-Day, San Francisco, Calif., 1964.
(31) For similar long range coupling constants in 3-pyrolines, see J. A. Deyrup, *J. Org. Chem.*, **34**, 2724 (1969); P. B. Woller and N. H. Cromwell, *J. Org. Chem.*, **35**, 888 (1970).
(32) It is conceivable that an *N*-benzylidene epoxide (e.g., **23**) is first formed and subsequently undergoes a rapid rearrangement to the 3-oxazoline system. However, we have not been able to detect such an intermediate in the early stages of the irradiation (i.e, <10% conversion).
(33) S. Sato, *Bull. Chem. Soc. Jpn.*, **41**, 1440 (1968).
(34) H. J. Bestmann and R. Kunstmann, *Chem. Ber.*, **102**, 1816 (1969).
(35) A. Mondon, *Justus Liebigs Ann. Chem.*, **603**, 115 (1957).
(36) K. V. Scherer, Jr., and R. S. Lunt, III, *J. Org. Chem.*, **30**, 3215 (1965).
(37) It was necessary to carry out the irradiation of **26a** in pentane which contained excess (2–5 mol) methanol since spiroazirine **26a** undergoes a rapid reaction with methanol in the dark to give 1-benzoylcyclopropylamine dimethyl acetal (see Experimental Section).
(38) N. R. Bertoniere and G. W. Griffin, "Organic Photochemistry" Vol. 3, O. L. Chapman, Ed., Marcel Dekker, New York, N.Y., 1973, p 115.
(39) G. W. Griffin and N. R. Bertoniere in "Carbenes", Vol. I, M. Jones and R. A. Moss, Ed., Wiley, New York, N.Y., 1973.
(40) C. L. Currie, H. Okabe, and J. R. McNesby, *J. Phys. Chem.*, **67**, 1494 (1963).
(41) P. A. Leermakers and G. F. Vesley, *J. Org. Chem.*, **30**, 539 (1965).
(42) G. W. Griffin, *Angew. Chem., Int. Ed. Engl.*, **10**, 537 (1971).
(43) W. Bauer and K. Hafner, *Angew. Chem., Int. Ed. Engl.*, **8**, 772 (1969).
(44) W. M. Jones, M. E. Stowe, E. E. Wells, Jr., and E. W. Lester, *J. Am. Chem. Soc.*, **90**, 1849 (1968), and references cited therein.
(45) W. M. Jones and C. L. Ennis, *J. Am. Chem. Soc.*, **89**, 3069 (1967).
(46) W. Kirmse, L. Horner, and H. Hoffmann, *Justus Liebigs. Ann. Chem.*, **614**, 19 (1958).
(47) A. W. Krebs, *Angew. Chem., Int. Ed. Engl.*, **4**, 10 (1965).
(48) A. Hassner, R. J. Isbister, R. B. Greenwald, J. T. Klug, and E. C. Taylor, *Tetrahedron*, **25**, 1637 (1969).
(49) Experiments are underway to spectroscopically detect azirinone **38** at low temperatures.
(50) W. Sieber, P. Gilger, S. Chaloupka, H. J. Hansen, and H. Schmid, *Helv. Chim. Acta*, **56**, 1679 (1973).
(51) It is conceivable that cycloadduct **44** is formed initially but rearranges to **43** under the reaction conditions. However, all attempts to detect **44** in the crude photolysate have failed, thus ruling out this possibility.
(52) J. Ciabattoni and M. Cabell, Jr., *J. Am. Chem. Soc.*, **93**, 1482 (1971).
(53) All melting points and boiling points are uncorrected. Elemental analyses were performed by Atlantic Microlabs, Atlanta, Ga. The infrared absorption spectra were determined on a Perkin-Elmer Model 137 Infracord spectrophotometer. The ultraviolet absorption spectra were measured with a Cary Model 14 recording spectrophotometer using 1-cm matched cells. The proton magnetic resonance spectra were determined at 100 MHz using a Jeolco-MH-100 spectrometer. Mass spectra were determined with a Perkin-Elmer RMU6 mass spectrometer at an ionizing voltage of 70 eV. All irradiations were carried out using a 450-W Hanovia medium-pressure mercury arc.
(54) W. E. Cass, *J. Am. Chem. Soc.*, **64**, 785 (1942).
(55) J. J. Basseller, C. Gueremy, and S. Julia, *Bull. Soc. Chim. Fr.*, 2988 (1965).
(56) A. Padwa, J. Smolanoff, and A. Tremper, *J. Am. Chem. Soc.*, **97**, 4682 (1975).
(57) D. M. Bailey, *Chem. Abstr.*, **75**, 129556p (1971).

Sulfur Isotope Effects in Substitution Reactions of Trimethylsulfonium Ion[1]

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Abstract: Sulfur isotope effects were determined for the SN2 reactions in ethanol at 60 °C of trimethylsulfonium ion with bromide, thiophenoxide, ethoxide, and phenoxide. The effects were 1.36, 1.20, 0.96, and 0.96%, respectively. The isotope effect with ethoxide in ethanol decreased upon addition of dimethyl sulfoxide. The decrease was almost linear with mole percent dimethyl sulfoxide, reaching a value of 0.35% at 65% dimethyl sulfoxide. These results suggest that the basicity of the attacking nucleophile is the most important factor in determining the extent of carbon–sulfur cleavage in the transition state.

The effect on transition-state structure of changes in reactant structure or reaction conditions is one of the central problems of physical organic chemistry. Two main theoretical approaches to this problem are currently in use: the Hammond postulate,[2] which is based on the idea that species of similar energy should have similar electronic structures, and the Swain–Thornton rule,[3] which considers the effects of perturbations on the normal modes of the transition state. Both theories predict that changing to a more reactive nucleophile in an SN2 reaction will give a more reactant-like transition state.

Difficulty in making unambiguous predictions arises