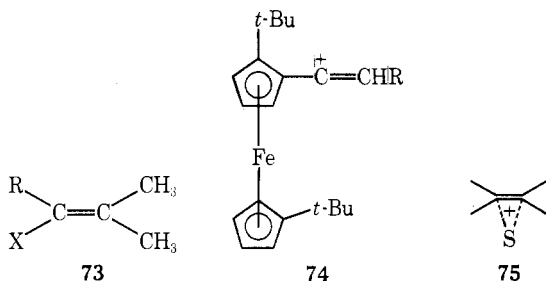


R = tolyl, phenyl) (fluorides and chlorides) labeled in various positions with a high concentration of ^{13}C were reacted with SbF_5 at low temperatures in nonnucleophilic solvents (SO_2ClF , CH_2Cl_2 , SO_2). If the aryl substituent in **73** is not an anisyl but a tolyl or a phenyl group, the results are less clear,⁴¹ though it has been reported that the phenyl vinyl chloride **73** (R = phenyl) can be converted into the corresponding vinyl cation.⁴² Our own results indicate moreover that there are serious differences between fluorides and chlorides and that,



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besides a vinyl cation, other still not identified species may be formed when arylvinyl chlorides of structure **73** (R = tolyl and phenyl, X = Cl) are reacted with SbF_5 .⁴¹

In addition to the above-mentioned experiments ferrocenylvinyl cations **74** were generated from ethynylferrocenes by protonation.⁴³ A direct NMR spectroscopic observation of such ferrocenylvinyl cations was possible in CF_3COOH solution if the reactive center was sterically shielded by a proximate *tert*-butyl group (**74**). Another example of the generation of a quite similar species to the vinyl cation is that of the thiarenium ion (**75**), a long-lived bridged vinyl cation.⁴⁴

My sincere thanks go to my co-workers who made this work possible. The financial support of several organizations such as the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and the Volkswagenstiftung, is gratefully acknowledged. I thank Dr. L. R. Subramanian and Dr. C. J. Liddiard for their help in preparing the manuscript.

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Azirine Photochemistry

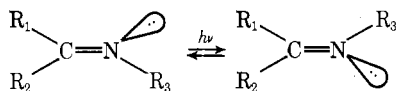
Albert Padwa

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Although kinetic and spectroscopic studies of the electronically excited carbonyl group are legion,¹ the photochemistry of the structurally related imine system has received little mechanistic attention. This is surprising in view of the many studies that have been made of the descriptive photochemistry of imines²⁻⁴ and of their spectroscopic behavior.⁵

The possibilities of both $n-\pi^*$ and $\pi-\pi^*$ excitation of this chromophore promise a variety of interesting physical and chemical conversion processes. While chemical reaction of the excited state of an imine has often been observed, a more frequently encountered phenomenon for simple imines is fast, efficient, radiationless deactivation. The low photoreactivity of the imine system can be attributed to rotation about the π bond in the excited state, which allows dissipation of electronic energy.⁶ In rigid systems, this mode of energy

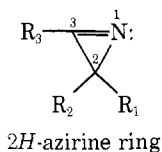


Albert Padwa was born in New York City in 1937. He received his B.A. and Ph.D. from Columbia University where he worked with Cheves Walling. After a year of postdoctoral work with Howard Zimmerman at the University of Wisconsin, he joined the Ohio State University faculty in 1963. In 1966 he moved to SUNY Buffalo, where he is now Professor of Chemistry. His research interests lie principally in the fields of organic photochemistry, molecular rearrangements, and the reactions of small-ring heterocyclic compounds.

dissipation is not available, and these cyclic imines have maximum opportunity to undergo reaction from an electronically excited state.

In 1970 we initiated an investigation of the photochemistry of small-ring cyclic imines, in which syn-anti photoisomerization about the C-N double bond should be a high-energy, structurally prohibited process.⁷ We were particularly interested in the three-membered azirine ring since this cyclic imine had been little studied except for a few instances in which either photodimerization^{8,9} or photorearrangement¹⁰ occurred. *2H*-Azirines are versatile substrates which can serve as useful precursors for the synthesis of other heterocyclic rings.¹¹

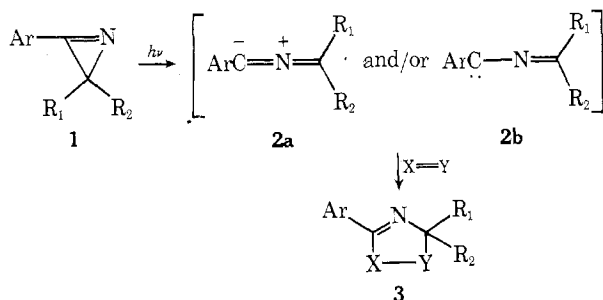
- (1) J. G. Calvert and J. N. Pitts, Jr., "Photochemistry", Wiley, New York, N.Y., 1966.
 (2) G. Wettermark in "The Chemistry of the Carbon-Nitrogen Double Bond", S. Patai, Ed., Interscience, New York, N.Y., 1969, p 565.
 (3) P. Beak and W. R. Messer, *Org. Photochem.*, **2**, 117 (1969).
 (4) A. Padwa, *Chem. Rev.*, in press.
 (5) M. A. El-Bayoumi, M. El-Aasser, and F. Abdel-Halim, *J. Am. Chem. Soc.*, **93**, 586 (1971).
 (6) A. Padwa and F. Albrecht, *J. Am. Chem. Soc.*, **94**, 1000 (1972); **96**, 4849 (1974); *J. Org. Chem.*, **39**, 2361 (1974).
 (7) A. Padwa and J. Smolanoff, *J. Am. Chem. Soc.*, **93**, 548 (1971).
 (8) F. P. Woerner, H. Reimlinger, and D. R. Arnold, *Angew. Chem., Int. Ed. Engl.*, **7**, 130 (1968).
 (9) F. P. Woerner and H. Reimlinger, *Chem. Ber.*, **103**, 1908 (1970).
 (10) E. F. Ullman and B. Singh, *J. Am. Chem. Soc.*, **88**, 1844 (1966); **89**, 6911 (1967).
 (11) F. W. Fowler, *Adv. Heterocycl. Chem.*, **13**, 45 (1971).



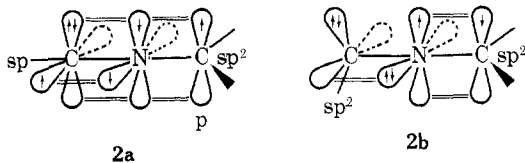
An unusual feature of this three-membered heterocyclic ring is that it is susceptible to attack by both electrophilic and nucleophilic reagents.¹¹ Also, the 2π electrons present in the ring can participate in thermally allowed [$\pi^4_s + \pi^2_s$] cycloadditions as dienophiles^{12,13} or as dipolarophiles.¹⁴

Generation of Nitrile Ylides

Independent studies by Padwa¹⁵ and Schmid¹⁶ have shown that 2H-azirines undergo irreversible ring opening on electronic excitation to give nitrile ylides as reactive intermediates. Nitrile ylides may be classified as nitrilium betaines, a class of 1,3 dipoles containing a central nitrogen atom and a π bond orthogonal to the 4π allyl system. They can be intercepted with a wide variety of dipolarophiles to form five-membered heterocyclic rings.



Among the possible forms of a nitrile ylide, a carbene structure (2b) can be envisaged which makes conceivable a 1,1 cycloaddition of this 1,3 dipole. Huisgen originally suggested that the bent geometric form (2b) of a nitrile ylide would be less stable than the linear form (2a), since allyl resonance would be at a maximum with the linear arrangement.¹⁷ The extensive literature



dealing with nitrile ylide cycloadditions has generally been explained in terms of the linear arrangement of this 1,3 dipole.¹⁸⁻³⁸ However, recent ab initio LCAO-

MO-SCF calculations by Salem³⁹ and Houk⁴⁰ indicate that the geometry of the nitrile ylide is appreciably different from that suggested by Huisgen.¹⁷ They conclude that the bent nitrile ylide geometry is favored over the linear geometry by at least 10 kcal/mol.

Substituted arylazirines exhibit strong ($\epsilon \sim 10,000$) ultraviolet absorption at ca. 240 nm with a weak inflection on the long-wavelength side of the principal absorption band (i.e., ca. 285 nm ($\epsilon \sim 500$)). This weak band shifts to shorter wavelengths with increasing polarity of the medium. By the empirical criteria of low intensity and blue shift in hydrogen-bonding solvents, this latter band can be attributed to an $n-\pi^*$ transition. The weakening of the C-C bond of the azirine ring as a result of this transition was attributed earlier¹⁰ to electrocyclic ring opening analogous to the cyclopropyl \rightarrow allyl cation rearrangement.

One may envisage the $n-\pi^*$ excitation process as leading to a species resembling structure 4, in which the nonbonding orbital on nitrogen contains only one electron. The electron that was promoted to the antibonding π^* orbital partially resides on the carbon atom, and consequently the nitrogen atom has become somewhat electrophilic and begins to resemble an aziridinylium cation. The remaining nonbonding electron on nitrogen, which is in the plane of the σ bonds of the ring, overlaps with the back lobe of the saturated carbon and facilitates bond scission. Electron demotion then results in the formation of nitrile ylide 2. A similar nonbonding orbital overlap with an adjacent σ bond has been postulated to account for the facile α cleavage (i.e., Norrish type I) encountered with carbonyl compounds.⁴¹

Schmid and coworkers^{23,38} report that irradiation of arylazirines in a rigid matrix at -185°C gives rise to a new maximum in the ultraviolet spectrum (ca. 350 nm) attributed to a nitrile ylide. Their results show that the dipole undergoes photochemical but not thermal reversion to the starting azirine. Irradiation of the azirine

(22) B. Jackson, M. Maerky, H. J. Hansen, and H. Schmid, *Helv. Chim. Acta*, **55**, 919 (1972); **55**, 748 (1972).

(23) W. Sieber, P. Gilgen, S. Chaloupka, H. J. Hansen, and H. Schmid, *Helv. Chim. Acta*, **56**, 1679 (1973).

(24) A. Orhovats, B. Jackson, H. Heimgartner, and H. Schmid, *Helv. Chim. Acta*, **56**, 2007 (1973).

(25) H. Heimgartner, P. Gilgen, U. Schmid, H. J. Hansen, H. Schmid, K. Pfoertner, and K. Bernauer, *Chimia*, **26**, 424 (1972).

(26) B. Jackson, N. Gakis, M. Maerky, H. J. Hansen, W. V. Philipborn, and H. Schmid, *Helv. Chim. Acta*, **55**, 916 (1972).

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(28) H. Giezendanner, H. J. Rosenranz, H. J. Hansen, and H. Schmid, *Helv. Chim. Acta*, **56**, 2588 (1973).

(29) N. S. Narasimhan, H. Heimgartner, H. J. Hansen, and H. Schmid, *Helv. Chim. Acta*, **56**, 1351 (1973).

(30) P. Gilgen, H. Heimgartner, and H. Schmid, *Helv. Chim. Acta*, **57**, 1382 (1974).

(31) U. Schmid, P. Gilgen, H. Heimgartner, H. J. Hansen, and H. Schmid, *Helv. Chim. Acta*, **57**, 1393 (1974).

(32) N. Gakis, H. Heimgartner, and H. Schmid, *Helv. Chim. Acta*, **57**, 1403 (1974).

(33) A. Orhovats, H. Heimgartner, H. Schmid, and W. Heinzmann, *Helv. Chim. Acta*, **57**, 2626 (1974).

(34) P. Gilgen, B. Jackson, H. J. Hansen, H. Heimgartner, and H. Schmid, *Helv. Chim. Acta*, **57**, 2634 (1974).

(35) N. Gakis, H. Heimgartner, and H. Schmid, *Helv. Chim. Acta*, **58**, 748 (1975).

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(14) V. Nair, *J. Org. Chem.*, **33**, 2121 (1968); *Tetrahedron Lett.*, 4831 (1971).

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(16) P. Claus, T. Doppler, N. Gakis, M. Georgarakis, H. Giezendanner, P. Gilgen, H. Heimgartner, B. Jackson, M. Marky, N. S. Narasimhan, H. J. Rosenkranz, A. Wunderli, H. J. Hansen, and H. Schmid, *Pure Appl. Chem.*, **33**, 339 (1973).

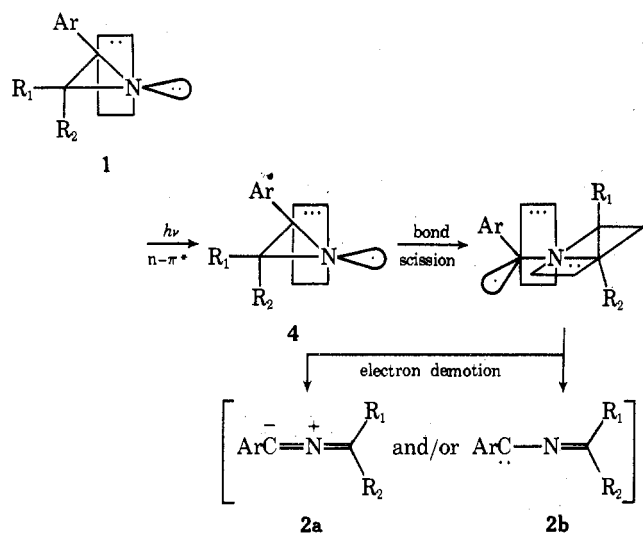
(17) R. Huisgen, *Angew. Chem., Int. Ed. Engl.*, **2**, 633 (1963).

(18) A. Padwa, M. Dharan, J. Smolanoff, and S. I. Wetmore, Jr., *J. Am. Chem. Soc.*, **94**, 1395 (1972); **95**, 1945, 1954 (1973).

(19) A. Padwa and S. I. Wetmore, Jr., *J. Org. Chem.*, **38**, 1333 (1973); **39**, 1396 (1974); *J. Am. Chem. Soc.*, **96**, 2414 (1974).

(20) A. Padwa, D. Dean, and J. Smolanoff, *Tetrahedron Lett.*, 4087 (1972).

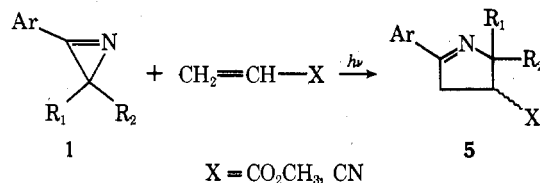
(21) H. Giezendanner, H. Heimgartner, B. Jackson, T. Winkler, H. J. Hansen, and H. Schmid, *Helv. Chim. Acta*, **56**, 2611 (1973).



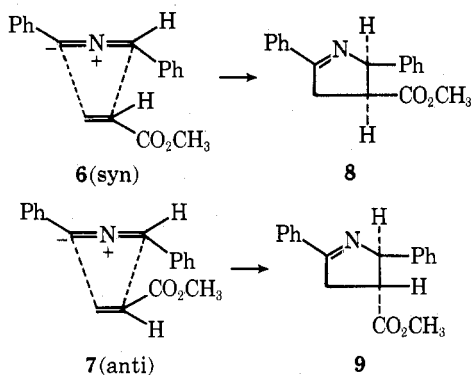
at $-185\text{ }^\circ\text{C}$ in the presence of a trapping agent also produced an absorption band at 350 nm. This band vanished, however, upon increasing the temperature to $-160\text{ }^\circ\text{C}$, thereby indicating that the cycloadduct is formed by thermal 1,3-dipolar addition of the initially generated nitrile ylide to the added dipolarophile.

Features of the Cycloaddition Process

The photocycloaddition of arylazirines with electron-deficient olefins to produce Δ^1 -pyrrolines^{18,19} exhibits all the characteristics of a concerted reaction, including stereospecificity and regioselectivity. 1,3-



Dipolar additions proceed via a "two-plane" orientation complex where the dipole and dipolarophile approach each other in parallel planes.⁴² For the case of diphenylazirine and methyl acrylate, two possible orientation complexes (6 or 7) exist. The interaction of substituent

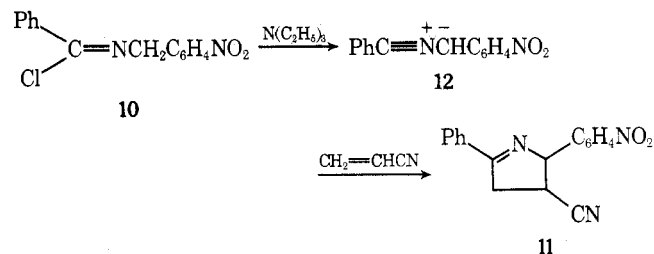


groups in the syn complex 6 can be of an attractive (π overlap, dipole-dipole interaction) or a repulsive nature (van der Waals strain). Both effects are negligible in the anti complex 7. The ratio of the products obtained gives insight into the interplay of steric and electronic substituent effects in the transition state of 1,3-dipolar addition and emphasizes the important role these ef-

(42) R. Huisgen, *J. Org. Chem.*, **33**, 2291 (1968); R. Huisgen, *Angew. Chem., Int. Ed. Engl.*, **2**, 565 (1963); *J. Org. Chem.*, **41**, 403 (1976).

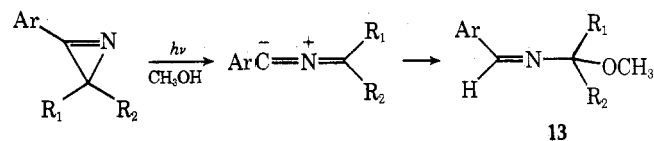
fects have in controlling the stereochemical distribution of the products obtained.¹⁸

The orientation of the groups in the Δ^1 -pyrrolines obtained from the photoaddition process is identical with that observed by Huisgen in related 1,3-dipolar additions.⁴² For example, treatment of *N*-(*p*-nitrobenzyl)benzimidoyl chloride (10) with triethylamine in the presence of acrylonitrile gives Δ^1 -pyrroline 11.⁴³ This reaction has been interpreted as proceeding via a nitrile ylide intermediate, 12.



Frontier molecular orbital theory correctly rationalizes the regioselectivity of most 1,3-dipolar cycloadditions.⁴⁴ When nitrile ylides are used as 1,3 dipoles, the dipole highest occupied (HOMO) and dipolarophile lowest unoccupied (LUMO) orbital interaction importantly stabilizes the transition state. The favored cycloadduct is that formed by union of the atoms with the largest coefficient in the dipole HOMO and dipolarophile LUMO. An electron-deficient olefin has the largest coefficient on the unsubstituted carbon in the LUMO.

In order to predict regioselectivity in the photocycloaddition of arylazirines, one must determine the relative magnitudes of the coefficients in the HOMO of the nitrile ylide. This problem was solved by carrying out the irradiation of several arylazirines in hydroxylic media.⁴⁵ The photoconversion of arylazirines (1) to alkoxyimines (13) indicates that in the HOMO of the nitrile ylide the electron density at the disubstituted carbon is greater than at the trisubstituted carbon atom.



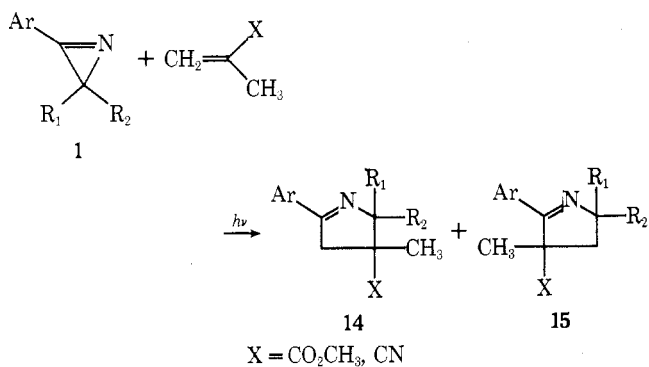
With this conclusion, all of the regiochemical data found in the photoaddition of arylazirines with dipolarophiles can be explained. Thus, acrylonitrile and methyl acrylate react with various nitrile ylides to give only 4-substituted regioisomers (5). Photocycloadditions of arylazirines with α -methylacrylonitrile and methyl methacrylate, on the other hand, give adducts of type 14 and 15 in a 3:2 ratio.¹⁸

The formation of a mixture of cycloadducts in this case can be attributed to enhancement of the LUMO coefficient at the unsubstituted carbon atom of the dipolarophile by the cyano or ester group, whereas the methyl group has the opposite effect.⁴⁴ The terminal coefficients in the LUMO of α -methylacrylonitrile and

(43) R. Huisgen, H. Stangle, H. J. Sturm, and H. Wagenhofer, *Angew. Chem., Int. Ed. Engl.*, **1**, 50 (1962); *Chem. Ber.*, **105**, 1258 (1972).

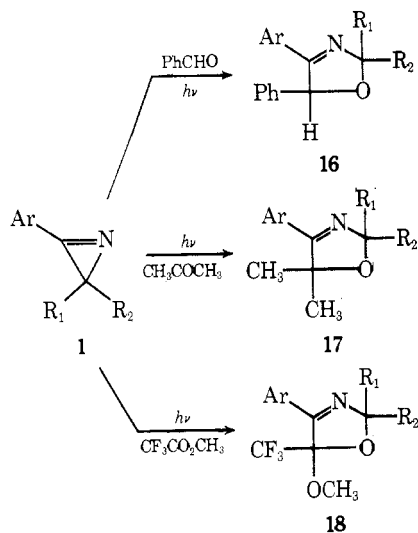
(44) K. N. Houk, J. Sims, R. E. Duke, R. W. Strozier, and J. K. George, *J. Am. Chem. Soc.*, **95**, 7287 (1973); **95**, 7301 (1973); **95**, 5798 (1973).

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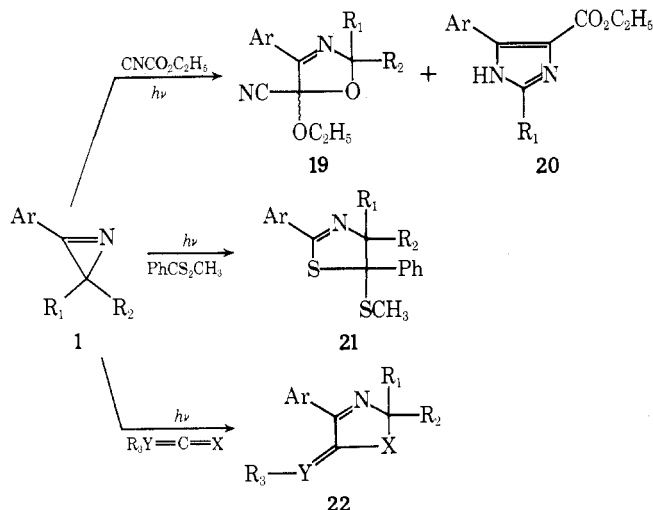


methyl methacrylate are more nearly the same than for the nonmethylated analogs, so that regioselectivity decreases for these dipolarophiles.

The photochemical addition of azirines to the carbonyl groups of aldehydes, ketones, and esters is also completely regioselective.¹⁹⁻²⁷ Besides the formation of



the isomeric oxazolines **19** from **1** and ethyl cyanofornate, there is also formed the imidazole **20** from addition to the C≡N bond in the expected regioselective manner.²² Thioesters lead to thiazolines²⁰ (**21**) while isocyanates and ketenes produce heterocycles (**22**).²⁶

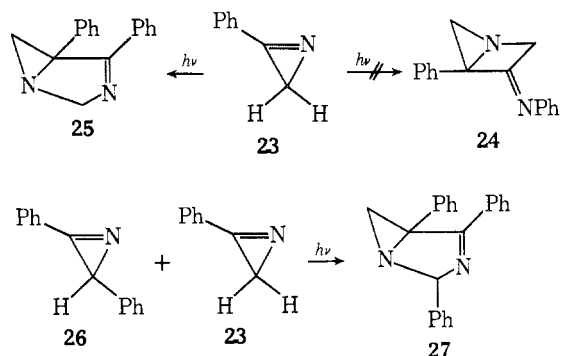


The photocycloaddition of arylazirines with a variety of multiple bonds proceeds in high yield and provides a convenient route for the synthesis of five-membered heterocyclic rings. Some of the dipolarophiles used in-

clude azodicarboxylates,³⁰ acid chlorides,³¹ vinylphosphonium salts,³² and *p*-quinones.³³

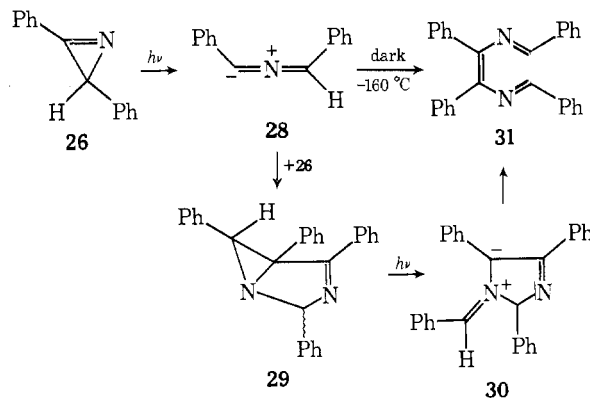
Photochemical Dimerizations of 2*H*-Azirines

Irradiation of arylazirines with olefins of low dipolarophilic activity produced no photoadduct but instead gave dimers.^{18,22,29} Originally it was reported that photolysis of phenylazirine (**23**) gave azabicyclopentane **24**.^{8,9} However, stimulated by the foregoing mechanistic rationale developed for the photolysis of azirines, it was shown that the photodimer is actually diazabicyclohexane (**25**). Thus, in the absence of an added dipolarophile, the nitrile ylide generated photochemically simply adds to the ground-state azirine molecule.¹⁸ A crossed dimerization of **26** to the ground state of **23** has also been realized.⁴⁶



Additional work showed that the photodimerization of arylazirines to 1,3-diazabicyclo[3.1.0]hex-3-enes is a general reaction which is independent of the nature of the substituent groups attached to the C atom of the azirine ring.^{19,26} Care is required in the choice of solvent, photolysis time, and substituents since the 1,3-diazabicyclohexenes are themselves photochemically labile.⁴⁷⁻⁴⁹

More recent work by the Zurich group³⁸ has shown that the nitrile ylide derived from diphenylazirine (**26**) also undergoes quantitative dimerization to 1,3,4,6-tetraphenyl-2,5-diaza-1,3,5-hexatriene (**31**) at -160°C . This result indicates that **31** is not only formed by the indirect route ($28 + 26 \rightarrow 29 \xrightarrow{h\nu} 30 \rightarrow 31$) but also by dimerization of **28** by a direct head to head coupling. The intermediacy of azomethine ylide **30** in the photochemical conversion of azabicyclohexene **29** to dia-



(46) A. Padwa, J. Smolanoff, and S. I. Wetmore, Jr., *J. Chem. Soc., Chem. Commun.*, 409 (1972).

(47) A. Padwa and E. Glazer, *J. Am. Chem. Soc.*, **94**, 7788 (1972); **92**, 1778 (1970); *Chem. Commun.*, 838 (1971).

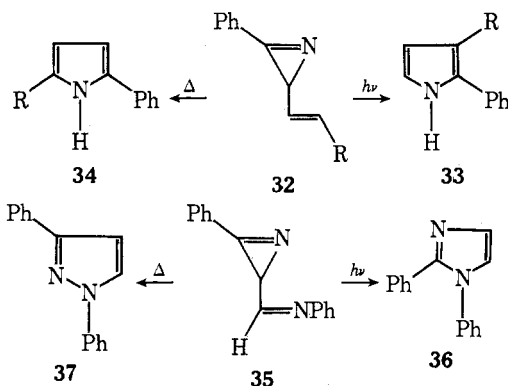
(48) A. Padwa and S. I. Wetmore, Jr., *J. Chem. Soc., Chem. Commun.*, 1116 (1972).

(49) R. Selvarajan and J. H. Boyer, *J. Heterocycl. Chem.*, **9**, 87 (1972).

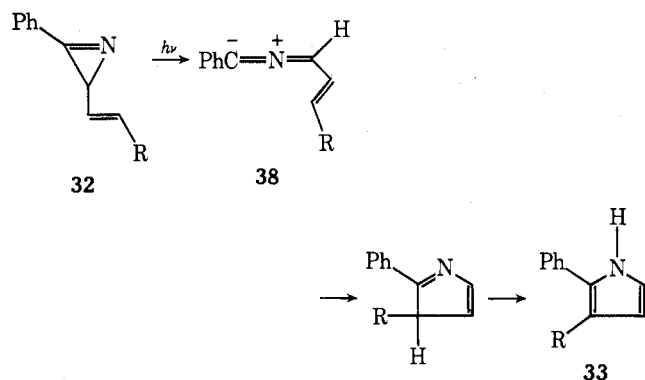
zahexatriene **31** was verified by low-temperature photolysis studies.

Intramolecular Cycloaddition Reactions of Vinyl-Substituted 2*H*-Azirines

Whereas the cycloaddition of arylazirines with simple olefins produces Δ^1 -pyrrolines, a rearranged isomer can be formed when the alkene and the azirine moieties are suitably arranged in the same molecule. We first observed this intramolecular photocycloaddition using 2-vinyl-substituted azirines.^{50,51} Irradiation of azirine **32** in benzene afforded a 2,3-disubstituted pyrrole (**33**), while thermolysis gave a 2,5-disubstituted pyrrole (**34**). Photolysis of azirine **35** proceeded similarly and gave 1,2-diphenylimidazole (**36**) as the exclusive photo-



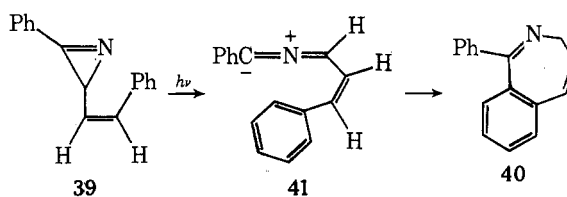
product. This stands in marked contrast to the thermal reaction of **35**, which afforded 1,3-diphenylpyrrole (**37**) as the only product.



The evidence obtained clearly indicates that the above photorearrangements proceed by a mechanism involving a nitrile ylide intermediate since cycloadducts could be isolated when the irradiations were carried out in the presence of trapping agents. Intramolecular cycloaddition of nitrile ylide **38** followed by a 1,3-sigmatropic hydrogen shift of the initially formed five-membered ring readily accounts for the formation of the final product.

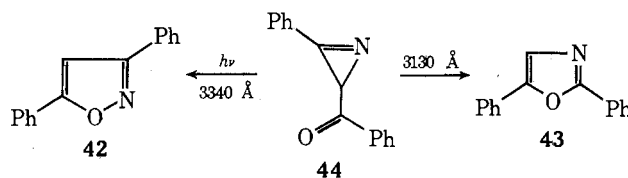
The thermal transformations observed with these systems can be rationalized in terms of an equilibration of the 2*H*-azirine with a transient vinylnitrene which subsequently rearranges to the 2,5-disubstituted pyrrole.

In contrast to the photochemical results encountered with **32**, the presence of a *cis*-styryl side chain in the 2 position of the azirine ring (**39**) leads to ring expansion



and gives benzazepine **40**. The 2-[2-(α - and β -naphthyl)vinyl]-3-phenyl-2*H*-azirine systems behaved similarly and proceeded with complete regioselectivity.⁵¹ The photolysis of the isomeric *trans*-styrylazirine follows an entirely different course and produces 2,3-diphenylpyrrole as the major product. This observation requires that opening of the azirine ring followed by intramolecular cyclization proceeds faster than isomerization about the C-C double bond. The formation of **40** indicates that the nitrile ylide obtained from **39** cyclizes more easily via a seven-membered transition state and leads to the preferential formation of benzazepine **40**. Cyclization of the nitrile ylide derived from the *trans* isomer to a seven-membered ring is precluded on structural grounds, and formation of 2,3-diphenylpyrrole occurs instead.

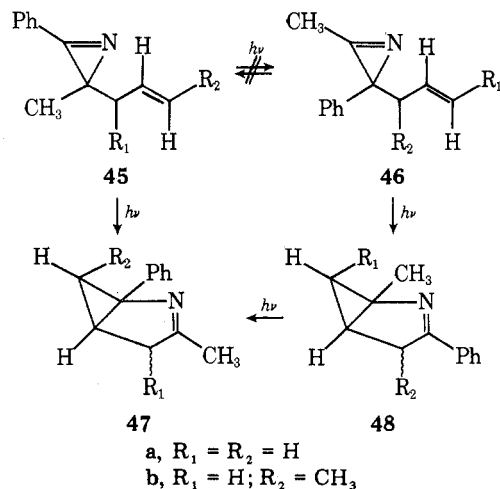
A reaction closely related to the above cyclizations was uncovered by Ullman and Singh in 1966.¹⁰ While studying the photochemical rearrangement of 3,5-diphenylisoxazole (**42**) to 2,5-diphenyloxazole (**43**), these workers observed the formation of an intermediate which proved to be 3-phenyl-2-benzoyl-2*H*-azirine (**44**). The photobehavior of azirine **44** was found to be dramatically controlled by the wavelength of the light used. With 3130-Å light, **44** rearranges almost quantitatively to oxazole **43**, whereas 3340-Å light causes rearrangement to isoxazole **42**. The formation of the isoxazole was



suggested to occur via the $n-\pi^*$ state of the carbonyl chromophore. Oxazole formation was attributed to selective excitation of the $n-\pi^*$ state of the azirine ring.

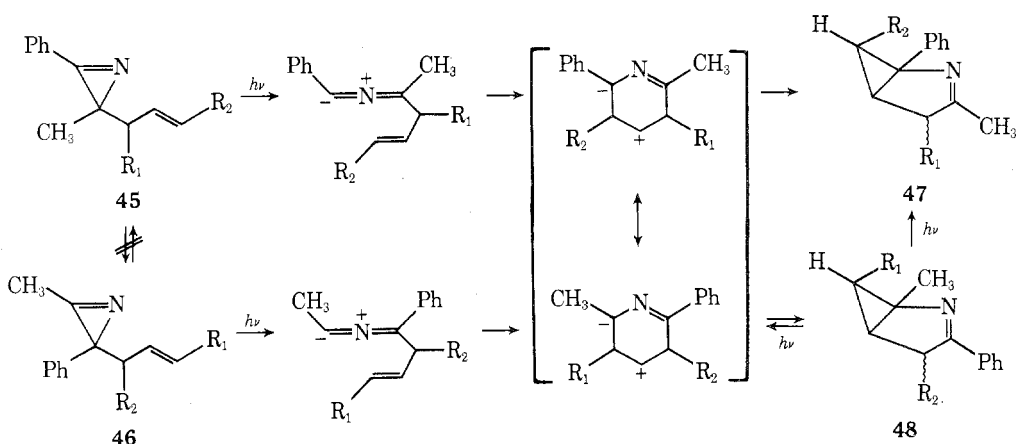
Intramolecular 1,1-Cycloaddition Reactions of 2*H*-Azirines

Having established that vinyl-2*H*-azirines undergo photochemical reorganization, we turned our attention



(50) A. Padwa, J. Smolanoff, and A. Tremper, *Tetrahedron Lett.*, 29 (1974); *J. Am. Chem. Soc.*, 97, 4682 (1975).

(51) A. Padwa and J. Smolanoff, *Tetrahedron Lett.*, 33, (1974).



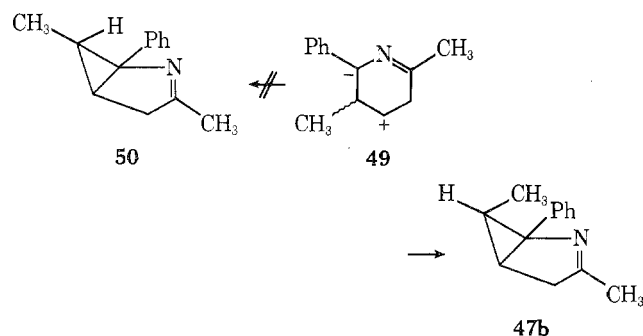
to the synthetic applications of the intramolecular cycloaddition reaction. Of particular interest was whether nitrile ylides could be intramolecularly added to double bonds in a 1,1 fashion. We uncovered the first example of such a process during an investigation of the photochemistry of 3-phenyl-2-methyl-2-allyl-2*H*-azirine (**45a**). Irradiation of **45a** gave a 1:1 mixture of azabicyclohexenes **47a** and **48a**.⁵² On further irradiation, **48a** was quantitatively isomerized to **47a**. Photolysis of **45a** in the presence of excess dimethyl acetylenedicarboxylate resulted in the 1,3-dipolar trapping of the normal nitrile ylide. Under these conditions, the formation of azabicyclohexenes **47** and **48** was entirely suppressed. The photoreaction of the closely related methyl-substituted azirine **45b** gave azabicyclohexene **47b** as the primary photoproduct. The formation of the thermodynamically less favored endo isomer (i.e., **47b**) corresponds to a complete inversion of stereochemistry about the π system in the cycloaddition process.

The photochemical behavior of the isomeric 3-methyl-2-phenyl-2-allyl-2*H*-azirine (**46a**) system was also studied.⁵³ Irradiation of **46a** in cyclohexane gave a quantitative yield of azabicyclohexenes **47a** and **48a**. Control experiments showed that **45** and **46** were not interconverted by a Cope reaction under the photolytic conditions. Photocycloaddition of **46** with an added dipolarophile afforded a different 1,3-dipolar cycloadduct from that obtained from **45**. The thermodynamically less favored endo isomer **47b** was also formed as the exclusive product from the irradiation of azirine **46b**.

As was pointed out earlier, 1,3-dipolar additions proceed via a "two-plane" orientation complex in which the dipole and dipolarophile approach each other in parallel planes. Inspection of molecular models of the allyl-substituted nitrile ylides indicates that the normal "two-plane" orientation approach of the nitrile ylide and the allyl π system is impossible as a result of the geometric restrictions imposed on the system. Consequently, the normal mode of 1,3-dipolar addition does not occur. In these systems, attack by the double bond is constrained to occur perpendicular to the plane of the nitrile ylide. The second LUMO, which is perpendicular to the ylide plane, is low-lying and presents a large vacancy at C-1 for attack by the more nucleophilic terminus of the neighboring double bond, without the possibility of simultaneous bonding at the C-3. This attack will generate a six-membered ring dipole which

contains a secondary carbonium ion as well as an azallyl anion portion. Collapse of this new 1,3 dipole will result in the formation of the observed azabicyclohexenes.

The photoconversion of the azabicyclohexenes (i.e., **48** \rightarrow **47**) can also be explained in terms of a six-membered ring dipole. The formation of the thermodynamically less favored endo isomer (**47b**) from photolysis of **45a** or **46b** can be attributed to the fact that collapse of the six-ring dipole (**49**) to the thermodynamically more favored exo isomer (**50**) will result in a severe torsional barrier on closure. Cyclization to the thermodynamically less favored endo isomer (**47b**) moves the phenyl and methyl groups increasingly further apart and accounts for the formation of the less stable product.



Several additional examples demonstrate the generality of the 1,1 trapping of nitrile ylides. Thus, treatment of *o*-allyl-substituted imidoyl chloride **51** with triethylamine gave benzobicyclo[3.1.0]hex-2-ene **52**.⁵⁴ Irradiation of the closely related methyl-substituted azirine system **53** gave a mixture of *endo*- and *exo*-benzobicyclohexenes (**54**) in quantitative yield.⁵⁴ No detectable quantities of the isomeric 1,3-dipolar adduct was observed in either system. In the case of **53**, the major product (*exo*-**54**) is the thermodynamically more favored exo isomer. The above systems provide additional support for the generality of 1,1 cycloadditions of nitrile ylides.

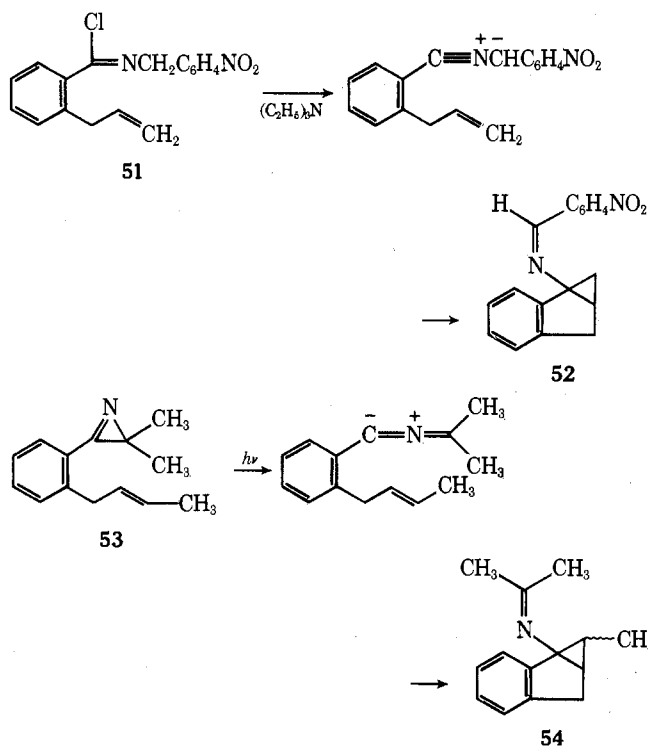
When the chain between the azirine ring and the alkene end is extended to three carbon atoms, the normal mode of 1,3-intramolecular dipolar cycloaddition occurs. For example, irradiation of azirine **55** gives Δ^1 -pyrroline **56** in quantitative yield.⁵⁵ In this case, the methylene chain is sufficiently long to allow the dipole

(52) A. Padwa and P. H. J. Carlsen, *J. Am. Chem. Soc.*, **97**, 3862 (1975).

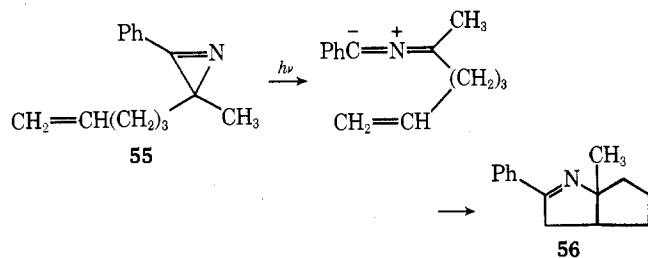
(53) A. Padwa and P. H. J. Carlsen, *J. Am. Chem. Soc.*, **98**, 2006 (1976).

(54) A. Padwa, A. Ku, A. Mazzu, and S. I. Wetmore, Jr., *J. Am. Chem. Soc.*, **98**, 1948 (1976).

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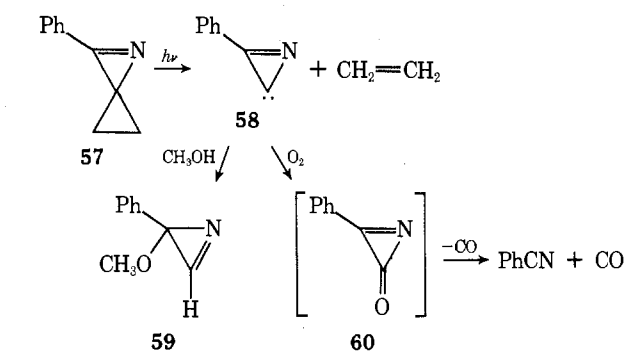
and olefinic portions to approach each other in parallel planes.



Further Reactions of 2H-Azirines

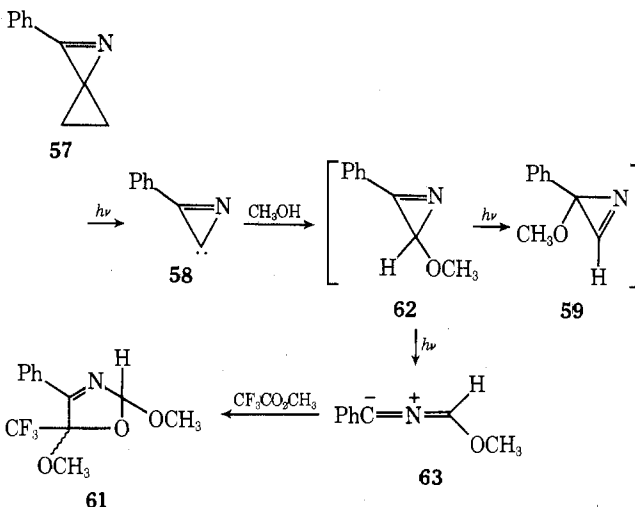
All of the reactions discussed above have involved the photocycloadditions of 2H-azirines with multiple π bonds. These studies have rigorously established nitrile ylides as useful intermediates in a variety of synthetic applications. More recent work from our laboratory has shown that the photolysis of certain 2H-azirines can lead to new and interesting photochemistry.

One of the most interesting examples involves 2-phenyl-1-azaspiro[2.2]pent-1-ene (57).⁵⁶ Irradiation of this spiroazirine in methanol results in a Griffin fragmentation⁵⁷ and produces ethylene and 2-phenylazirinyldene (58). This novel carbene undergoes subsequent reaction with methanol to produce 2-methoxy-2-phenyl-2H-azirine (59). When the irradiation of 57 is carried out in the presence of oxygen, benzonitrile and carbon monoxide are formed. In the absence of oxygen, an extremely small quantity of benzonitrile is formed and is presumably derived by competitive cycloelimination from 57. The formation of benzonitrile can be attributed to the intermediacy of 2-phenylazirone (60) as a transient intermediate. Hassner and Taylor have previously shown that aziriones are unstable and



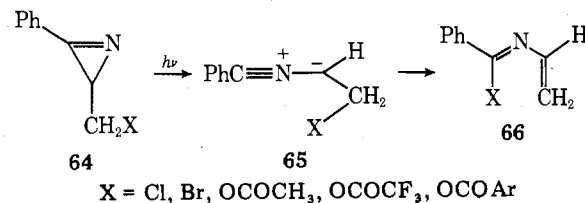
readily lose carbon monoxide to form nitriles,⁵⁸ thereby providing good analogy for this reaction.

Irradiation of spiroazirine 57 in pentane solution in the presence of both methanol and methyl trifluoroacetate (excess)⁵⁹ produced only a mixture of the two stereoisomers of 3-oxazoline 61. This result suggests that 2-phenylazirinyldene (58) reacts with methanol to give mainly azirine 62, which is subsequently converted to nitrile ylide 63 (and thus cycloadduct 61) on



further irradiation. The formation of azirine 59 could be explained by a photoinduced methoxy migration of 62 which competes with C-C bond cleavage of the azirine ring. Ciabattini and Cabell⁶⁰ previously reported that 2-chloro-2H-azirines undergo ready isomerization at room temperature via a 2π -electron azacyclopropenyl cation. A similar mechanism would rationalize the apparent photoconversion of azirines 62 and 59.

Irradiation of a series of hydroxymethyl-2H-azirine derivatives (64) which contain good leaving groups was found to give N-vinylimines (66) via a novel 1,4-substituent shift.⁶¹ The results indicate that the migrating



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(59) A. Padwa, J. K. Rasmussen, and A. Tremper, *J. Am. Chem. Soc.*, **98**, 2605 (1976).

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(57) G. W. Griffin and N. R. Bertoni in "Carbenes", Vol. I, M. Jones and R. A. Moss, Ed., Wiley, New York, N.Y., 1973.

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substituent (X) must be a reasonably good leaving group in order for the rearrangement to occur. Involvement of a nitrile ylide intermediate (65) in these reactions was demonstrated by trapping experiments. The quantum efficiency and rate of reaction were shown to be directly related to the leaving group ability.

Conclusion

The photocycloaddition reaction of 2*H*-azirines is an extremely versatile and important process. The range of synthetic possibilities which it opens for the construction of five-membered heterocyclic rings is ex-

tremely large. Significant progress has been made toward understanding the factors which determine the photochemical behavior in a given system. Since it is evident that nitrile ylides are very important species for the synthesis of a wide variety of nitrogen-containing compounds, we are continuing our efforts to develop new and useful applications of 2*H*-azirine photochemistry.

It is a pleasure to acknowledge the vital contribution of my collaborators, whose names are to be found in the references. Together, we thank the National Science Foundation and the National Institutes of Health for financial support of our research.

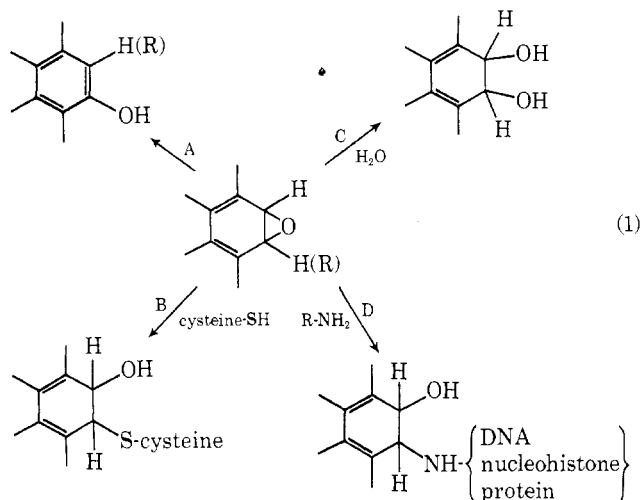
Solution Chemistry of Arene Oxides

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The inherent chemical interest in the chemistry of the epoxides of aromatic hydrocarbons (arene oxides) is heightened by their importance in biochemistry and toxicology (eq 1). Thus, arene oxides are: (1) proven or proposed intermediates in the biosynthesis (path A) of



After dropping out of high school to serve in the military, Thomas C. Bruice attended the University of Southern California (B.S., 1950, Ph.D., 1954) and received his postdoctoral training at UCLA. Prior to moving to University of California, Santa Barbara, in 1964, Professor Bruice held faculty positions in biochemistry at Yale University Medical School and the Johns Hopkins School of Medicine and in chemistry at Cornell University. In 1974 he was elected a member of the National Academy of Sciences. His research has involved the study of the mechanisms of reactions of biochemical interest.

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various metabolically important phenols (i.e., phenylalanine \rightarrow tyrosine, tryptophan \rightarrow 5-hydroxytryptophan \rightarrow serotonin, 4-hydroxyphenylpyruvic acid \rightarrow homogentisic acid, etc.);¹ (2) intermediates in aromatic compound detoxification via the biosynthesis of mercapturic acids² (path B) and dihydro diols (path C);³ and (3) proven causative agents of necrosis,⁴ mutagenesis,⁵ and carcinogenesis^{6,7} as a result of covalent binding to cellular macromolecules (path D). Recent reviews have dealt with the biochemical and toxicological aspects of aromatic epoxides and their chemical synthesis.^{1,3,8}

Examination of eq 1 reveals that the biologically important reactions of arene oxides may be divided into the categories of epoxide rearrangement (A) and nucleophilic addition (B–D). This Account is limited to our investigations of the mechanism of arene oxide rearrangement to phenols, the susceptibility of arene oxides to nucleophilic addition, and the differences in the chemistry of K-region and non-K-region epoxides. The K region of aromatic hydrocarbons does not possess full aromatic character, and its excision from a molecule does not greatly alter the resonance energy.⁹ Historically, those polycyclic hydrocarbons possessing K regions have been associated with carcinogenesis.

General Acid Catalysis and the Stepwise Conversion of Arene Oxides via Carbocations to Phe-

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