2,5-Di-*t*-butylpyrazine (48). To 4.00 g of 1-azido-3,3-dimethyl-1-butene (**45**)[14a] was added 20 ml of a 2% sodium methoxide solution and 60 ml of absolute methanol. The reaction mixture was photolyzed for 21.5 hr. Removal of the solid from the clear solution produced a yellow semisolid. To this solid was added *ca.* 125 ml of ether and *ca.* 100 ml of water. The water was separated and the ethereal solution washed again with *ca.* 100 ml of water. The ethereal solution was dried, and removal of the solvent with reduced pressure gave 2.10 g of a pale yellow liquid. Methanol (30 ml) and 10 ml of a 10% HCl solution were added to this liquid. The reaction mixture immediately turned a deep red color which slowly decolorized within 10 min. The reaction mixture stood at room temperature for 14 hr, and removal of the solvent with reduced pressure and heating gave a yellow oil. This was dissolved in water (*ca.* 50 ml) and was neutralized with 20% NaOH solution. After standing 2 days at room temperature, the solution yielded yellow crystals. These were filtered giving 0.961 g of 2,5-di-*t*-butylpyrazine, mp 104–106°, identical with those recovered from photolysis of 1-azido-3,3-dimethyl-1-butene in pentane. Recrystallization from pentane gave the analytical sample: mp 110–110.5°; nmr ($CDCl_3$) τ 1.39 (s, 2, ring protons) and 8.60 (s, 18, $C(CH_3)_3$).

Anal. Calcd for $C_{12}H_{20}N_2$: C, 74.95; H, 10.48. Found: C, 75.27; H, 10.34.

***cis*-2-Methyl-3-phenylaziridine (52).** To 1.00 g of lithium aluminum hydride in 50 ml of absolute ether was added slowly 2.62 g of 3-methyl-2-phenyl-1-azirine (**8**) in 15 ml of absolute ether. The reaction mixture was stirred for 4 hr, and the excess lithium aluminum hydride was decomposed with 20% NaOH solution (2 ml). The salts were filtered, and removal of the ether gave 2.55 g of a pale yellow liquid which crystallized, mp 37–38°. Recrystallization from pentane gave a pure sample: mp 40.5–41° (lit.[29] 41–43°); phenylcarbamoyl derivative, mp 92.5–93° (lit.[29] 92–94°).

***cis*-2,3-Diphenylaziridine (54).** To 1.00 g of lithium aluminum hydride in 50 ml of absolute ether was added slowly 1.93 g of 2,3-diphenyl-1-azirine in 15 ml of absolute ether. The reaction mixture was stirred overnight, and the excess lithium aluminum hydride was decomposed with a 20% NaOH solution (*ca.* 2 ml). The salts were filtered, and removal of the solvent gave 1.63 g of colorless crystals, mp 74–78°. Recrystallization from methanol gave a pure sample, mp 81–82° (lit.[32] 83°); phenylcarbamoyl derivative, mp 165–166° (lit.[29] 163–164°).

9-Azabicyclo[6.1.0]nonane (55). To 1.50 g of lithium aluminum hydride in 80 ml of absolute ether was added 3.41 g of 9-azabicyclo-[6.1.0]non-1(9)-ene (**12**). The reaction mixture was stirred for 14 hr. The excess lithium aluminum hydride was decomposed with 2.5 ml of a 20% NaOH solution. The salts were filtered, and removal of the solvent gave 2.62 g of a colorless liquid. The picrate derivative was recrystallized from ethanol, mp 203–207° (lit.[33] 190–195°); phenylthiocarbamoyl derivative, mp 133–133.5° (lit.[33] 132–133°). The picrate derivative was identical with an authentic sample prepared by reduction of 1-azido-2-iodooctane with lithium aluminum hydride.[22a]

9-Azabicyclo[6.1.0]non-2-ene (57). To 0.75 g of lithium aluminum hydride in 50 ml of absolute ether was added 1.254 g of 9-azabicyclo[6.1.0]nona-1(9),2-diene (**13**) in 8 ml of absolute ether. The reaction mixture was stirred for 5 hr, and the excess lithium aluminum hydride was decomposed with a 20% NaOH solution (*ca.* 2 ml). The salts were filtered, and removal of the ether gave 1.010 g of a pale yellow liquid, picrate mp 169–171°, recrystallized from methanol, mp 170–172°. The infrared spectrum of the picrate was identical with that prepared from the reduction of 3-azido-4-iodocyclooctene, mp 170–172°.[22a]

Acknowledgment. This work was supported by U. S. Public Health Service Grant CA-04474 from the National Cancer Institute.

(32) D. A. Darapsky and J. Spannagle, *J. Prakt. Chem.*, **92**, 272 (1915).

(33) D. V. Kashelikar and P. E. Fanta, *J. Am. Chem. Soc.*, **82**, 4927 (1960).

The Reaction of 1-Azirines with Acid Chlorides. A Potential Route to the 2-Azirine Ring System[1a,b]

F. W. Fowler[1c] and Alfred Hassner

Contribution from the Department of Chemistry, University of Colorado, Boulder, Colorado 80302. *Received November 18, 1967*

Abstract: Benzoyl chloride reacted with 3-methyl-2-phenyl-1-azirine (**3**) in acetone at 5° to give ring-expanded oxazole **4** and ring-opened dichloro amide **5**. By carrying out the reaction in refluxing benzene, it was possible to obtain the intermediate N-benzoyl-2-chloroaziridine **6** resulting from addition of the reagent to the C=N. Benzoyl chloride in refluxing benzene reacted with 2,3-diphenyl-1-azirine (**9**) and fused azirine **14** to give chloroaziridines **10** and **15**. Chloroaziridines **6** and **10** were solvolyzed in polar solvents giving oxazoles **4** and **11** and smaller amounts of the dichloro amides **5** and **12**. Benzenesulfonyl chloride reacted with azirine **3** to yield the ring-opened sulfonamides **17** and **18**, whereas azirine **9** was inert to benzenesulfonyl chloride in pyridine. Azirines **3** and **9** were unreactive toward alkyl halides in refluxing acetone and were insoluble in dilute hydrochloric acid. The low basicity of azirines was found to be in accord with the high percentage of s character (35.6) of exocyclic bonds in this ring system as measured by the carbon-13–hydrogen coupling constant (176 Hz) of 3-phenyl-1-azirine. Attempted dehydrochlorination of **6** and **10** using either 1,4-diazabicyclo[2.2.2]octane (DABCO), potassium *t*-butylate, or sodium hydride did not give the anticipated 2-azirine derivative. Chloroaziridine **6** was unreactive toward DABCO and sodium hydride, whereas chloroaziridines **6** and **10** reacted with potassium *t*-butylate to produce 1-azirines **3** and **9** and *t*-butyl benzoate. These results along with the anomalous reaction of 1-azirines with Grignard reagents to give aziridines are discussed in terms of the antiaromaticity of the 2-azirine ring system.

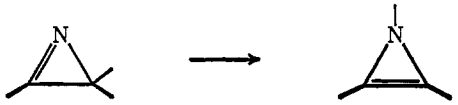
Because of the previous inaccessibility of the 1-azirine ring system,[2] very few of these compounds have been known and their chemical reactivity has received little attention. With the recent discovery in our laboratory of a general synthesis of 1-azirines

(1) (a) Stereochemistry. XXXIII. Chemistry of Small Rings. XV. For paper XXXII, see A. Hassner and F. W. Fowler, *J. Am. Chem. Soc.*, **90**, 2869 (1968); (b) a preliminary account of this work was reported at the First International Symposium on Heterocyclic Chemistry, Albuquerque, N. M., 1967; (c) NASA Predoctoral Fellow, 1965–1967.

(2) The nomenclature of azirines in the recent literature has been confusing. The system proposed by the Ring Index (the H nomenclature) is cumbersome and not readily recognizable to most chemists. We suggest the use of 1-azirine instead of 2H-azirine. For example, i should be called 2-methyl-1-azirine and not methylazirine, 2-methyl-

from olefins,[3] it has been possible to initiate an exploratory study of this unsaturated three-membered ring.

One of the more intriguing aspects of 1-azirines (**1**) is their potential conversion into the isomeric 2-azirines (**2**). The 2-azirine ring system is of theoretical interest since it is a necessarily planar π system containing four electrons and, according to Hückel's rule, would not be predicted to be stabilized by delocalization.[4] Furthermore, four-π-electron systems have been referred to as being antiaromatic.[5]



1 **2**

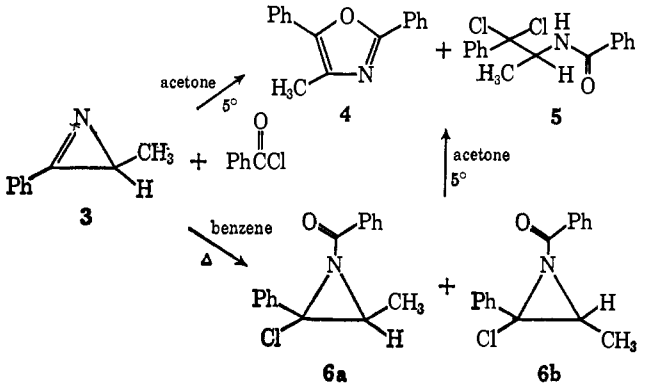
Breslow and coworkers[5b] have recently discussed the concept of antiaromaticity and its apparent manifestation in the instability of certain cyclic conjugated systems such as cyclobutadiene and the cyclopropenyl anion. The cyclopropenyl anion is predicted to be an antiaromatic ion since simple HMO calculations for the allyl anion (DE = 0.83β) and the cyclopropenyl anion (DE = 0.00β) show that changing from linear to cyclic conjugation results in destabilization. This destabilization is apparently the reason for the slow rate of deuterium exchange in 1,2-diphenyl-3-benzoylcyclopropene compared to the corresponding cyclopropane derivative.

Simple Hückel calculations[6] on enamine (DE = 0.30β) and 2-azirine (DE = 0.00β) also predict that the change from linear to cyclic conjugation results in destabilization and therefore 2-azirine is also predicted to be an antiaromatic compound.

Since the addition of acid halides to the 1-azirine ring system followed by the elimination of hydrogen chloride appeared to provide a feasible route to the 2-azirine ring system, this reaction was investigated in detail.

Results

Benzoyl chloride and 3-methyl-2-phenyl-1-azirine (**3**) reacted at 5° in acetone to give mainly 2,5-diphenyl-4-methyloxazole (**4**) and a smaller amount of amide **5**.[7] If the reaction was carried out in refluxing benzene rather than in acetone, a pale green oil was obtained which, from physical and chemical data, appeared to be a mixture of the stereoisomeric N-benzoylchloroaziridines **6a** and **b** in a ratio of 6:4. This assignment was based on the appearance of two methyl doublets in the nmr spectrum, the more intense one appearing at τ 8.90 shifted upfield from the other one by 0.57 ppm. This is probably due to the magnetic anisotropic effect of the phenyl substituent at C-3 which shields the *cis* methyl group shifting its absorption upfield.[8] Chloroaziridine **6a** is also the isomer expected from steric considerations; that is, the approach of reagents to the C=N should occur *trans* to the methyl substituent at C-2. This view is strengthened by the recent discovery of the stereospecific addition of hydride to 1-azirines.[3] The absorption of the amide carbonyl in **6** occurs at 1698 cm^{-1} and is also consistent with the three-membered ring structures.



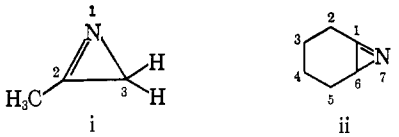
Although the appearance of two doublets for the methyl group of **6** could be due to slow inversion of the lone pair of electrons on nitrogen, this is unlikely, since it is known that N-acetylaziridine does not show line broadening until below −120°.[9] An attempt to run the nmr spectrum at high temperatures resulted in rearrangement to oxazole **4**.

All attempts to purify chloroaziridines **6** by either chromatography or crystallization only led to rearranged products.

Chloroaziridines **6a** and **b**, when dissolved in acetone and kept at 5°, rearranged to oxazole **4** and amide **5**. They were formed in the same molar ratio as was previously observed in the direct reaction of benzoyl chloride and azirine **3** in acetone. The structure of chloro amide **5** was proven by conversion to the known N-benzoyl-α-aminopropiophenone (**8**).[10] Keto amide **8** was independtently synthesized by first hydrolyzing azirine **3** to α-aminopropiophenone and then treating this salt with benzoyl chloride in pyridine.

Treatment of aziridine **6** with phenylmagnesium bromide gave 2,2-diphenyl-3-methylaziridine (**7**) thus establishing the three-membered structure for **6**. The structure of aziridine **7** was proven by comparison with an authentic sample prepared from the reaction of 3-methyl-2-phenyl-1-azirine with phenylmagnesium bromide.

azirene or 3-methyl-2H-azirine. Fused azirine ii would be 7-azabicyclo-[4.1.0]hept-1(7)-ene.



i ii

(3) A. Hassner and F. W. Fowler, *Tetrahedron Letters*, 1545 (1967); ref. 1a.

(4) The substitution of a heteroatom, such as nitrogen, for an ethylenic linkage in a planar, conjugated cyclic system perturbs the system only slightly and does not invalidate Hückel's rule. See M. E. Volpin, *Russ. Chem. Rev.*, **29**, 129 (1960).

(5) (a) R. Breslow, *Chem. Eng. News*, 90 (June 28, 1965); (b) R. Breslow, J. Brown, and J. J. Gajewski, *J. Am. Chem. Soc.*, **89**, 4383 (1967).

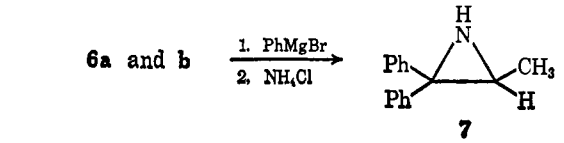
(6) A. Streitwieser, Jr., "Molecular Orbital Theory for Organic Chemists," John Wiley and Sons, Inc., New York, N. Y., 1961, p 135. The parameters used here were as follows: $\alpha_N = \alpha_C + 1.5\beta$; $\beta_{C-N} = \beta_{C-C}$.

(7) While this work was in progress the reaction of 2-phenyl-1-azirine with acyl chlorides to give the corresponding 2-substituted 5-phenyloxazoles was reported: S. Sato, H. Kato, and M. Ohta, *Bull. Chem. Soc. Japan*, **40**, 1014 (1967).

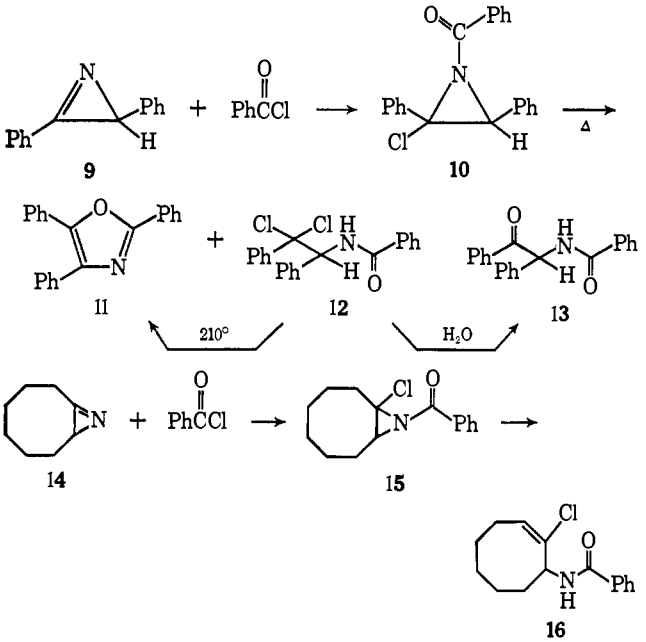
(8) Similar results were observed with *cis*- and *trans*-2-phenyl-3-methylaziridines. The *cis* isomer has its doublet absorption centered at τ 9.47 shifted upfield 0.30 ppm from the *trans* isomer. See P. J. Brois, *J. Org. Chem.*, 27, 3532 (1962); J. L. Pierre and P. Arnaud, *Bull. Soc. Chim. France*, 1040 (1966).

(9) F. A. L. Anet, R. Trepka, and D. J. Cram, *J. Am. Chem. Soc.*, **89**, 357 (1967).

(10) G. H. Cleland and C. Niemann, *ibid.*, **71**, 841 (1949).



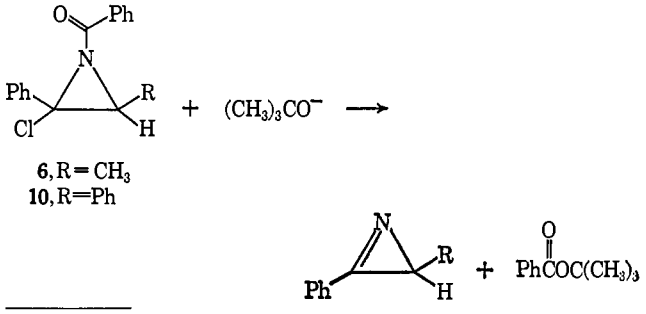
Benzoyl chloride also underwent reaction with 2,3-diphenyl-1-azirine (**9**) and 9-azabicyclo[6.1.0]non-1(9)-ene (**14**) to give the corresponding N-benzoylchloroaziridines **10** and **15**. Both of these N-benzoylchloroaziridines showed strong carbonyl absorptions at *ca.* 1700 cm^{-1}. The nmr spectrum of **10** showed only one singlet for the ring proton indicating only one stereoisomer which is consistent with the larger size of phenyl compared to methyl substituents. *Thus, the addition of benzoyl chloride to 1-azirines in benzene appears to be general for the synthesis of N-benzoyl-2-chloroaziridines.*



Chloroaziridine **10** in methanol underwent a similar rearrangement as did **6** in acetone. The structure of chloro amide **12** was evident from spectral data and its conversion to the known keto amide **13**.[11]

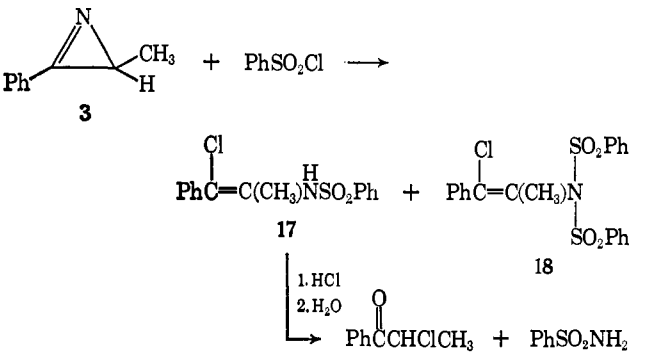
N-Benzoylchloroaziridine **15** when pyrolyzed in methanol gave only the unsaturated amide **16** and no oxazole. The structure of **16** was evident from its elemental analysis and infrared and nmr spectra (see Experimental Section).

Chloroaziridine **6** was unreactive toward DABCO in ether and sodium hydride in 1,2-dimethoxyethane. Chloroaziridines **6** and **10** did react with potassium *t*-butylate in ether to give a 1:1 mixture of *t*-butyl benzoate and azirines **3** and **9**.

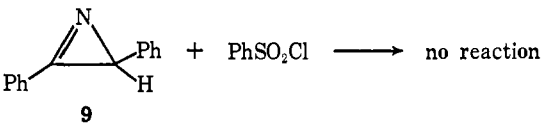


(11) D. Davidson, M. Weiss, and M. Jelling, *J. Org. Chem.*, **2**, 319 (1937).

When azirine **3** was treated with an excess of benzenesulfonyl chloride in pyridine, a mixture of sulfonamides **17** and **18** was produced. Sulfonamide **18** was undoubtedly formed from **17** and excess benzenesulfonyl chloride since this type of transformation is known[12] and has been shown to occur under the reaction conditions. The structures of sulfonamides **17** and **18** are



supported by elemental analysis and infrared and nmr spectra. Also, sulfonamide **17** could be cleaved to α-chloropropiophenone and benzenesulfonamide with hydrogen chloride. Interestingly, azirine **9** is unreactive toward benzenesulfonyl chloride in pyridine.



Discussion

It was predicted that the addition of alkyl halides across the carbon–nitrogen double bond of 1-azirines followed by elimination of HX could be a suitable method for the synthesis of the 2-azirine ring system.[13] However, 2,3-diphenyl-1-azirine and 3-methyl-2-phenyl-1-azirine were unreactive toward either methyl iodide or benzyl chloride in refluxing acetone.

This lack of reactivity is undoubtedly due to the very low basicity of 1-azirines. The endocyclic orbitals of three-membered rings have a greater amount of p character than in larger rings in order to better accommodate the compressed bond angles.[14] This increase of p character in the endocyclic orbitals results in an increase in s character in the exocyclic orbitals. As the per cent s character of an orbital containing a lone pair of electrons increases, a decrease in basicity is observed. For example, the low basicity of pyridine (sp^2) compared to other tertiary amines is well known.

Measurement of the carbon-13–hydrogen coupling constant is a method, although recently criticized,[15] which has been used to determine the per cent s character in the exocyclic orbitals of small heterocyclic and carbocyclic rings.[16] The carbon-13–hydrogen coupling

(12) J. Cason and H. Rapoport, "Laboratory Text in Organic Chemistry," Prentice-Hall Inc., Englewood Cliffs, N. J., 1962, p 240.

(13) Simple chloroaziridines have recently been prepared and when treated with sodium methoxide solvolysis reactions rather than elimination of hydrogen chloride occurred. Other methods for elimination of hydrogen chloride were not reported. See R. B. Greenwald and J. A. Deyrup, *J. Am. Chem. Soc.*, **87**, 4538 (1965).

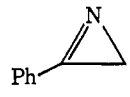
(14) (a) D. Peters, *Tetrahedron*, **19**, 1539 (1963); (b) C. A. Coulson and T. H. Goodwin, *J. Chem. Soc.*, 3161 (1963).

(15) (a) D. M. Grant and W. M. Lichtman, *J. Am. Chem. Soc.*, **87**, 3994 (1965); (b) G. J. Karabatsos and L. E. Orzech, Jr., *ibid.*, **86**, 3574 (1964).

(16) (a) D. Seebach, *Angew. Chem. Intern. Ed. Engl.*, **4**, 123 (1965); (b) F. S. Mortimer, *J. Mol. Spectry.*, **5**, 199 (1960).

constant of 2-phenyl-1-azirine (**19**) indicates *ca.* 36% rather than the expected 25% s character (sp^3) for the carbon–hydrogen orbitals at position 2. Now if there is a corresponding increase of s character for the orbital (sp^2) containing the lone pair of electrons on nitrogen then this orbital should approach 50% s character (sp). If this is the case, then the basicity of 1-azirines would be similar to that of nitriles which also have their lone pair of electrons in an orbital of *ca.* 50% s character (sp).

Although the basicity of 1-azirines does not appear to be as low as that of nitriles, 3-methyl-2-phenyl-1-azirine is insoluble in 10% hydrochloric acid solution. This azirine is soluble in 37% hydrochloric acid and neutralization after 5 min with 20% potassium hydroxide solution gave a 47% recovery of the azirine by nmr analysis. The azirinium ion **20** is probably relatively stable since most if not all of the decomposition presumably occurred in the neutralization step.



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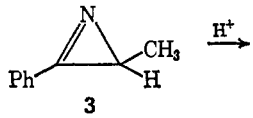

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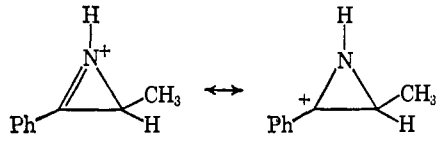

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The value of $J_{^{13}C-H}$ for azirine **19** is larger than the value calculated for a carbocyclic analog, cyclopropene. This is probably due to two factors. First, the expected shorter C=N compared to the C=C in these three-membered rings will cause a decrease in the internal bond angle of the saturated carbon atom of azirine **19** with respect to cyclopropene. To accommodate this decrease in bond angle, azirine **19** will contribute more p character to the endocyclic orbitals than cyclopropene. This will result in a larger percentage of s character for the exocyclic orbitals of azirine **19**. In addition, the saturated carbon atom of azirine **19** should undergo a slight rehybridization, compared to cyclopropene, in order to concentrate more p character in the orbital directed toward the more electronegative nitrogen atom.[17] This should result in a slight increase of s character for the exocyclic orbitals of the saturated carbon atom in azirine **19**. This latter effect is probably the reason for the large value of $J_{^{13}C-H}$ for ethylenimine compared to cyclopropane.

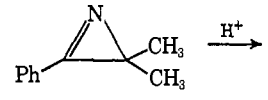
Table I

Compound	$J_{^{13}C-H}$ for CH_2, cps	s character, %
Cyclopropane	161	32.2[a]
Cyclopropene	166	33.2[b]
Ethylenimine	166	32.2[c]
Azirine **19**	176	35.6

[a] N. Muller and D. E. Pritchard, *J. Chem. Phys.*, **31**, 768, 1471 (1959). [b] C. S. Foote, *Tetrahedron Letters*, 579 (1963); P. H. Kasai, R. J. Myers, D. F. Eggers, Jr., and K. B. Wiberg, *J. Chem. Phys.*, **30**, 512 (1959). [c] Reference 16b.

The electrophilic reagent benzoyl chloride did react with azirine **3** but oxazole **4** and amide **5** were formed rather than the chloroaziridine when acetone was used as a solvent.

Leonard and coworkers have recently reported a related ring-expansion reaction of 1-azirines.[18] They have observed that when anhydrous perchloric acid is generated in acetone in the presence of 2-phenyl-3,3-dimethyl-1-azirine (**21**), ring opening to the protonated oxazoline **23** occurs. This represents a formal cleavage of the 1,3 carbon–nitrogen single bond of 1-azirines whereas we observe only cleavage of the 1,2 carbon–nitrogen double bond.



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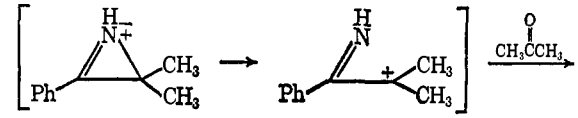

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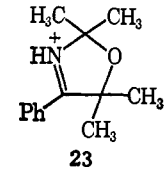

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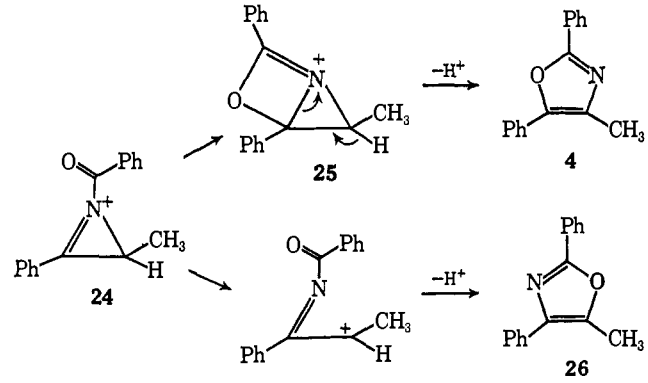
There are two mechanistic pathways that can be envisioned for the reaction of benzoyl chloride with 1-azirine **3** to give oxazole **4**. One involves the formation of azirinium ion **24** which can rearrange and, after loss of a proton, lead to the oxazole. However, azirinium ion **24** is analogous to the azirinium ion **22** postulated by Leonard and would be expected to rearrange to the isomeric oxazole **26**. In addition, this pathway does not rationalize the formation of amide **5**.



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24

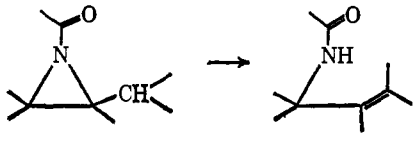
26

The possibility that azirinium ion **24** rearranges to the observed oxazole through structure **25** as either a discrete intermediate or transition state appears unlikely but has not been ruled out.

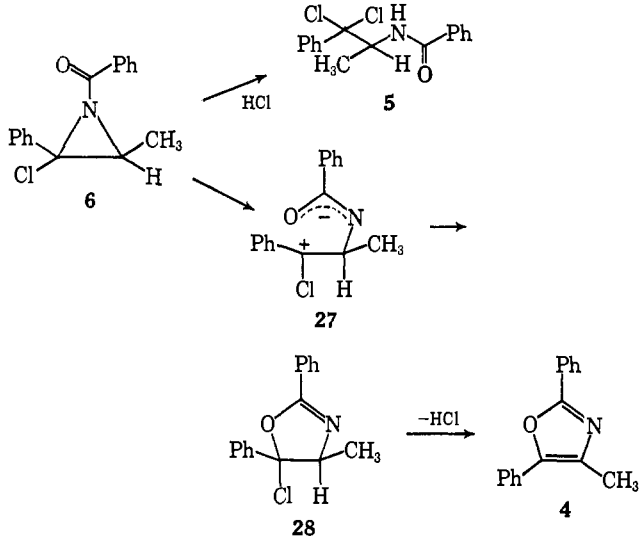
A more attractive mechanism would involve the chloroaziridine **6** as an intermediate since N-benzoyl-

(17) H. A. Bent, *Chem. Rev.*, **61**, 275 (1961).

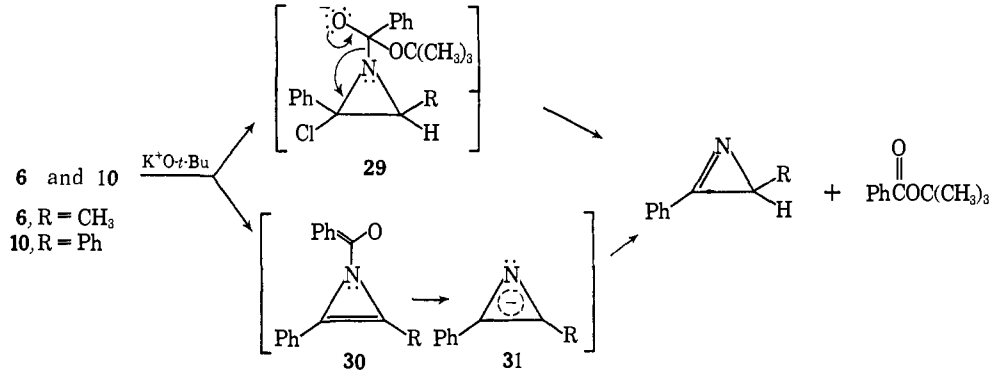
(18) N. J. Leonard and B. Zwanenburg, *J. Am. Chem. Soc.*, **89**, 4456 (1967).



aziridines are known to rearrange to oxazolines when heated.[19] The oxazoline in this case could easily lose hydrogen chloride to give the aromatic oxazole. Amide **5** could be formed on ring opening of **6** by hydrogen chloride.



This view is supported by the observation that the chloroaziridine was isolated if the reaction was carried out in a nonpolar solvent such as benzene. Also, this chloroaziridine rearranged when placed in acetone at 5° to give the same molar ratio of oxazole **4** and amide **5** that was observed in the direct reaction of azirine **3** with benzoyl chloride in acetone.



The thermal rearrangement of N-acylaziridines has been extensively studied by Fanta[20] and coworkers who observed that not all N-acylaziridines rearrange to 2-oxazolines. If a side-chain proton is available then a pyrolytic *cis* elimination takes place giving an N-allyl amide.

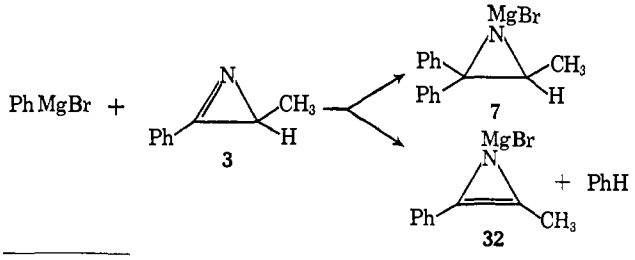
The necessary side-chain proton is available in aziridine **6** and yet we observed no unsaturated amide formation. This is explainable in terms of an ionic mechanism which has recently been postulated for such rearrangements.[20] The ionic intermediate **27** for the rearrangement of aziridine **6** to oxazoline **28** would be stabilized significantly by the presence of the phenyl and chloro substituents at C-2.[21] Thus, in our case oxazoline formation has probably become very favorable relative to unsaturated amide formation.

Consistent with solvolysis to the ionic intermediate **27** is the observation that the chloroaziridine can be isolated if the reaction is carried out in a nonpolar solvent such as benzene.

Chloroaziridine **10** when heated in methanol gave an equimolar mixture of oxazole **11** and amide **12**. However, chloroaziridine **15** when heated in methanol did not give an oxazole. Instead, rearrangement to the N-allyl amide **16** occurred. Apparently, the presence of a stabilizing substituent such as a phenyl group at position two is necessary for oxazole formation, in accord with the ionic mechanism.

When N-benzoylchloroaziridines **6a** and **b**, apparent precursors for the synthesis of 2-azirine derivatives, were treated with sodium hydride or DABCO no reaction took place. Treatment of either chloroaziridines **6** or **10** with a much stronger base, potassium *t*-butylate, produced the 1-azirine and *t*-butyl benzoate. This result can be rationalized in terms of either the intermediate complex **29** which can fragment to give the observed products or, alternatively, the desired 2-azirine. Cleavage of the 2-azirine would be expected to yield *t*-butyl benzoate and an azirinyl anion. Protonation of this azirinyl ion should give the presumably thermodynamically more stable 1-azirine **3**.

We have observed as have Eguchi and Ishii[22] that 1-azirines react with Grignard reagents to give aziridines. Thus **3** led to 2,2-diphenyl-3-methylaziridine (**7**). This is an anomalous reaction of ketimines.[23] Generally, the Grignard reagent abstracts an α-hydrogen giving the enamine which on work-up produces the starting imine. Since the enamine in this case would be **32**, a derivative of a 2-azirine, the failure to obtain such a product in the reaction of 1-azirine **3** with Grignard reagents suggests that the 2-azirine system is unstable.



(19) H. W. Heine, *Angew. Chem. Intern. Ed. Engl.*, **1**, 528 (1962).
(20) P. E. Fanta and E. N. Walsh, *J. Org. Chem.*, **31**, 59 (1966).
(21) A. Streitwieser, *Chem. Rev.*, **56**, 573 (1956).
(22) S. Eguchi and Y. Ishii, *Bull. Chem. Soc. Japan*, **36**, 1434 (1963).
(23) R. W. Leyer, *Chem. Rev.*, **63**, 489 (1963).

We also attempted to synthesize a N-benzenesulfonylchloroaziridine by the addition of benzenesulfonyl chloride across the 1-azirine carbon–nitrogen double bond. Unfortunately, the reaction of benzenesulfonyl chloride with 3-methyl-2-phenyl-1-azirine in pyridine gave only sulfonamides **17** and **18**. Again, the chloroaziridine may be an intermediate in this reaction since it is known that N-benzenesulfonylaziridines also rearrange to unsaturated amide on pyrolysis.[24]

Frequently, the reason given for the inability to synthesize a four-π electron cyclobutadiene system from cyclobutene derivatives was that the added double bond introduced too much strain energy. This argument cannot be applied to the four-π-electron 2-azirine system since 1-azirines which should have about the same strain energy are readily synthesized. Possibly our inability to synthesize the 2-azirine ring system and the reaction of Grignard reagents with 1-azirines to give aziridines rather than 2-azirine indicate that the cyclic conjugation results in destabilization.

Experimental Section[25]

Reaction of 3-Methyl-2-phenyl-1-azirine (3) with Benzoyl Chloride in Acetone. To 1.31 g of 3-methyl-2-phenyl-1-azirine was added 20 ml of dry acetone and 1.41 g of benzoyl chloride. The reaction mixture was kept at 5° for 24 hr during which time a yellow solid precipitated. Removal of the solvent gave a yellow solid that when treated with water gave an oil that crystallized. This solid was collected and air dried to give 2.51 g of pale yellow crystals. The nmr spectrum ($CDCl_3$) showed this to be 25% amide **5** and 75% 2,5-diphenyl-4-methyloxazole (**4**). This mixture was dissolved in 100 ml of absolute ether, and gaseous HCl was passed through the solution. A colorless solid precipitated which was collected and treated with water to give 1.32 g of colorless crystals, mp 75–76°. Recrystallization from Skellysolve B (bp 60–70°) gave 1.19 g, mp 80–81° which proved to be 2,5-diphenyl-4-methyloxazole (lit.[26] 81–82°).

Anal. Calcd for $C_{16}H_{15}N$: C, 81.66; H, 5.57. Found: C, 81.94; H, 5.70.

The solvent from the filtrate after treatment with gaseous HCl was removed giving a yellow oil which slowly crystallized when triturated with Skellysolve **B** (bp 60–70°). The crystals were collected giving 0.443 g, mp 74–81°. Recrystallization for cyclohexane and Skellysolve **B** gave pure amide **5**, mp 85–86°; nmr ($CDCl_3$) τ 2.0–2.8 (m, 5, aromatics), 3.4–3.8 (m, 1, NH), 4.6–4.9 (m, 1, C*H*CH_3), and 8.68 (d, 3, J = 6.5 Hz).

N-Benzoyl-2-phenyl-2-chloro-3-methylaziridine (6). To 2.62 g (0.02 mol) of 3-methyl-2-phenyl-1-azirine was added 2.82 g (0.02 mol) of benzoyl chloride and 50 ml of dry benzene. The reaction mixture was refluxed for 48 hr. The solvent was then removed at reduced pressure and warming (*ca.* 65°) to give 5.68 g of a pale yellow oil. The nmr spectrum ($CDCl_3$) showed this to be a mixture of the two stereoisomers, **6a** and **6b**, with signals at τ 2.89–3.89 (m, 10, aromatics), 6.4–6.8 (m, 1, C*H*CH_3), 8.33, 8.90 (two doublets, J = 6 Hz for both, with a total integration of three protons, CHC*H*$_3$, in a ratio of 4:6); ir 1698 cm^{-1} (C=O).

Rearrangement of 6 in Acetone. To 475 mg of chloroaziridine **6** was added 10 ml of dry acetone. The reaction mixture was kept at 5° for 24 hr. Removal of the solvent gave an oil which when treated with water produced a yellow solid. This was collected giving 456 mg of a pale yellow solid. The nmr spectrum was identical with that of the product obtained from the direct reaction of benzoyl chloride and 3-methyl-2-phenyl-1-azirine. They both show *ca.* 25% of amide **5** and 75% of oxazole **4**.

Reaction of 6 with Hydrogen Chloride in Ether. To 1.602 g of the chloroaziridine **6** was added 50 ml of absolute ether. Gaseous HCl was passed through the solution, and within *ca.* 30 sec a precipitate began to develop. The reaction mixture was stoppered and allowed to stand at room temperature for 5 hr. The colorless precipitate was filtered and treated with water giving 0.723 g, mp 77–79°. Recrystallization from Skellysolve B (bp 60–70°) and cyclohexane gave 0.343 g, mp 81.5–82.5°, of oxazole **4**.

Removal of the solvent from the filtrate after gaseous HCl treatment gave 0.820 g of a yellow oil. Trituration of this oil with Skellysolve **B** produced pale yellow crystals. These were filtered and dried, mp 83–85°. Recrystallization from Skellysolve **B** gave an analytical sample of amide **5**, mp 85–86°.

Anal. Calcd for $C_{15}H_{15}NOCl_2$: C, 62.35; H, 4.91. Found: C, 62.78; H, 5.13.

Acid Hydrolysis of 5. To 150 mg of **5** was added 7 ml of methanol followed by 1 ml of a 20% HCl solution. The reaction mixture was refluxed for 24 hr and was then poured into *ca.* 100 ml of water. This was neutralized with 20% NaOH and an oil precipitated which slowly crystallized giving 92 mg of a colorless solid. The nmr spectrum ($CDCl_3$) showed this to be a 43:57 mixture of oxazole **4** and amide **5**.

These could be separated by preparative thin layer chromatography using pH 7 silica gel and eluting with a 3:2 mixture of benzene and ether. The first band proved to be oxazole **4** and the second N-benzoyl-α-aminopropiophenone (**8**). The amide was identical with an authentic sample (see below).

N-Benzoyl-α-aminopropiophenone (8). To 1.31 g of 3-methyl-2-phenyl-1-azirine (**3**) was added 15 ml of methanol and 3 ml of 10% HCl solution. The reaction mixture turned slightly orange. Refluxing the reaction mixture for 3 hr followed by removal of the solvent left an orange solid. This solid was recrystallized from methanol–ethyl acetate giving 1.50 g of pale yellow crystals of α-aminopropiophenone hydrochloride, mp 191–193° subl and dec (lit.[26] 182°).

To 0.516 g of α-aminopropiophenone hydrochloride was added 10 ml of pyridine and 1.00 g of benzoyl chloride. The reaction mixture remained at room temperature for 12 hr and was then poured into water. An oil precipitated which slowly crystallized giving 0.620 g of colorless crystals: mp 103–104° (lit.[10] 104–105°); nmr ($CDCl_3$) τ 1.8–2.8 (m, 11, aromatics and NH), 4.23 (quintet, 1, J = 7 Hz, C*H*CH_3), and 8.47 (d, 3, J = 7 Hz).

N-Benzoyl-2-chloro-2,3-diphenylaziridine (10). To 1.93 g of 2,3-diphenyl-1-azirine was added 15 ml of dry benzene and 1.41 g of benzoyl chloride. The reaction mixture was refluxed and removal of the solvent gave a quantitative yield of the N-benzoyl-2-chloro-2,3-diphenylaziridine; nmr ($CDCl_3$) τ 1.9–3.1 (m, 10, aromatics), 5.5 (s, 1, C*H*Ph); ir (CCl_4, smear) 1700 cm^{-1} (C=O).

N-Benzoyl-1-chloro-9-azabicyclo[6.1.0]nonane (15). To 1.23 g of 9-azabicyclo[6.1.0]non-1(9)-ene was added 15 ml of benzene and 1.41 ml of benzoyl chloride. The reaction was refluxed for 14 hr. Removal of the solvent gave 2.513 g of the chloroaziridine **15**. The infrared spectrum showed a strong absorption at 1698 cm^{-1} (C=O).

Pyrolysis of N-Benzoyl-2,3-diphenylchloroaziridine 10 in Methanol to 12. To 6.68 g of the chloroaziridine **10** was added methanol and this was immediately removed with heating (*ca.* 70°) under reduced pressure until a solid formed. This was then treated with hot cyclohexane and cooled. Filtration of the colorless solid gave 3.02 g of a product, mp 147–151°. The analytical sample of **12** was obtained by recrystallization from methanol: mp 166.5–167°; nmr ($CDCl_3$) τ 2.1–3.1 (m, 16, aromatics and NH), 3.94 (d, 1, J = 9 Hz, C*H*PhNH).

Anal. Calcd for $C_{15}H_{17}Cl_2NO$: C, 68.12; H, 4.63. Found: C, 68.40; H, 5.00.

The solvent was removed from the above filtrate giving a brown solid. One crystallization from methanol gave 2.13 g of colorless needles, mp 113–115°. A pure sample was obtained by recrystallization from methanol, mp 115–115.5° (lit.[27] 114–115°). A mixture melting point with an authentic sample of 2,4,5-triphenyloxazole showed no depression.[28]

Hydrolysis of Amide 12 to N-Desylbenzamide (13). To 549 mg of **12** was added 25 ml of methanol and 5 ml of 10% HCl solution. The reaction was refluxed for 48 hr, and then *ca.* two-thirds of the solvent was removed producing colorless crystals. These were collected and recrystallized from ethanol, 178 mg, mp 128–130°.

(24) D. V. Kashelikar and P. E. Fanta, *J. Org. Chem.*, **26**, 1941 (1961).

(25) All melting points were determined on a Fisher-Johns melting point block and are uncorrected. Infrared spectra were recorded with a Perkin-Elmer IR-21 spectrometer. Nuclear magnetic resonance spectra were recorded with a Varian A-60 or A-60A spectrometer. Microanalyses were performed by either A. Berhardt, Mulheim Germany, or Galbraith Laboratories, Knoxville, Tenn. In nmr descriptions, s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet.

(26) J. Lister and R. Robinson, *J. Chem. Soc.*, **101**, 1297 (1912).

(27) G. Kirchner, *Ann.*, **628**, 92 (1959).

(28) A. Schonberg, *Ber.*, **54**, 242 (1921).

Recrystallziation from methanol raised the melting point to 140–141° (lit.[11] 141°).

N-Benzoyl-2-chloro-3-aminocyclooctene (16). To 5.52 g of **15** was added *ca.* 150 ml of methanol. The methanol was then stripped off at reduced pressure (*ca.* 15 mm) with heating. A light brown oil was produced which could be crystallized by triturating with cyclohexane. This gave 2.72 g of tan crystals, mp 99–104°. One recrystallization from cyclohexane gave 1.84 g of colorless crystals, mp 115–116°. The analytical sample was prepared by recrystallization from methanol: mp 116–117°; ir (KBr) 3322 (NH), 1642 and 1536 cm^{-1} (amide I and amide II bands); nmr ($CDCl_3$) τ 2.1–2.4 (m, 2, aromatics), 2.5–2.8 (m, 3, aromatics), 3.25 (broadened d, 1, J = 8 Hz, NH), 4.05 (t, 1, J = 8.5 Hz, C=C*H*), 4.60 (q, 1, J = 8 Hz, C*H*NH), 7.5–9.0 (m, 10, cyclooctyl ring protons).

Anal. Calcd for $C_{15}H_{18}ClNO$: C, 68.23; H, 6.90; N, 5.35. Found: C, 68.41; H, 6.79; N, 5.22.

Reaction of N-Benzoyl-2-chloro-2-phenyl-3-methylaziridine with Potassium *t*-Butylate. To 1.402 g of **6** was added 15 ml of dry ether. This was added to a slurry of 1.5 g of potassium *t*-butylate in 15 ml of cold ether (*ca.* 5°). The reaction was kept cold for 20 min and then washed with water. The aqueous extracts were combined and extracted with ether. These were combined with the original ether extracts and dried. Removal of the ether gave 1.348 g of a pale yellow liquid. The nmr spectrum of this product showed it to be a 1:1 mixture of 3-methyl-2-phenyl-1-azirine and *t*-butyl benzoate. The azirine was separated from *t*-butyl benzoate by dissolving the reaction mixture in ether and passing gaseous HCl through the solution. This precipitated the azirine giving an ethereal solution of *t*-butyl benzoate.

Reaction of N-Benzoyl-2-chloro-2,3-diphenylaziridine (10) with Potassium *t*-Butylate. To 0.930 g of chloroaziridine **10** was added 10 ml of dry ether and 1.0 g of potassium *t*-butylate. After 15 min, the reaction mixture was washed with water and dried with magnesium sulfate. Removal of the ether under reduced pressure gave 0.978 g of an orange oil. The nmr spectrum showed a 1:1 mixture of *t*-butyl benzoate and 2,3-diphenyl-1-azirine. Again the azirine could be separated from *t*-butyl benzoate by dissolving the reaction mixture in ether and passing gaseous HCl through the solution. The azirine precipitates giving an ethereal solution of *t*-butyl benzoate.

2,4,5-Triphenyloxazole from Amide 12. The pyrolysis of 263 mg of amide **12** was carried out on a melting point block at 210° for 1.5 hr. The brown oil remaining was triturated with methanol producing a quantitative yield of 2,4,5-triphenyloxazole, mp 109–111°. Recrystallization from methanol produced a pure sample of the oxazole, mp 115–115.5°. A mixture melting point with an authentic sample of 2,4,5-triphenyloxazole showed no depression.[28]

2,2-Diphenyl-3-methylaziridine (7). To 0.972 g of magnesium in a round-bottomed flask was added *ca.* 2 g of bromobenzene in 3 ml of absolute ether. As soon as the reaction had begun additional bromobenzene (total weight 6.28 g) and 25 ml of absolute ether were added. As soon as the reaction had ceased 1.31 g (0.01 mol) of 3-methyl-2-phenyl-1-azirine was added. An exothermic reaction took place. After the reaction had stood at room temperature for 6 hr it was poured into saturated ammonium chloride solution. This was extracted with ether. The ethereal extracts were combined and dried with $MgSO_4$. Anhydrous gaseous HCl was passed through the ethereal solution producing the amine hydrochloride which was collected and dried, 2.01 g, mp 141.5–143° (lit.[29] 142–143°).

Treatment of this salt with ammonia produced the free base, mp 71–72° (lit.[29] 72–73°).

2,2-Diphenyl-3-methylaziridine from 6. To 0.50 g of magnesium in 3 ml of ether was added *ca.* 2.0 g of bromobenzene. As soon as a reaction occurred, the remaining bromobenzene was added (total 3.95 g) followed by 20 ml of ether. The reaction was refluxed for 15 min and 1.36 g of **6** was added in 5 ml of ether. The reaction was refluxed for 19.25 hr, then poured into 50 ml of saturated ammonium chloride solution, and extracted with ether. The ethereal extracts were dried and passage of gaseous HCl through the solution produced an oil. Treatment of this oil with 10% ammonia solution produced the free amine which was extracted with ether. The ethereal extracts were combined and dried. Removal of the ether with reduced pressure gave 0.47 g of pale yellow crystals, mp 64–69°. Several recrystallizations from pentane gave colorless crystals, mp 70–71° (lit.[29] 72–73°), infrared spectrum identical with 2,2-diphenyl-3-methylaziridine (**7**) prepared from 3-methyl-2-phenyl-1-azirine and phenylmagnesium bromide.

Reaction of 3-Methyl-2-phenyl-1-azirine (3) with Benzenesulfonyl Chloride to 17 and 18. To 2.62 g of 3-methyl-2-phenyl-1-azirine was added 25 ml of pyridine and 8 ml of benzenesulfonyl chloride. The reaction mixture was allowed to stand at room temperature for 17.5 hr and then poured into 100 ml of 20% hydrochloric acid. This was extracted with ether. The ether extracts were dried. Removal of the ether under reduced pressure gave 3.67 g of a colorless solid, mp 102–106°. Treatment of this with 60 ml of 5% KOH solution left a colorless solid which was filtered, 1.29 g, mp 148–150°. The analytical sample of **18** was obtained form methanol–tetrahydrofuran: mp 156–158°; nmr ($CDCl_3$) τ 2.1–2.9 (m, 15, aromatics), 8.20 (s, 3, CCH_3); the ir (KBr) spectrum showed no NH absorption.

Anal. Calcd for $C_{21}H_{19}NClS_2O_4$: C, 56.30; H, 4.05; N, 3.13. Found: C, 56.05; H, 4.23; N, 3.31.

Neutralization of the above filtrate with 10% HCl solution gave 2.24 g of a colorless solid, mp 102–110°. Recrystallization from benzene–cyclohexane gave the analytical sample of **17**, mp 115–116°. The nmr spectrum ($CDCl_3$) of the crude product (mp 102–110°) showed two singlets at τ 7.83 and 8.03 with a relative ratio of 1:3 indicating the presence of two isomers. Recrystallization yielded one stereoisomer: mp 115–116°; nmr ($CDCl_3$) τ 2.1–2.8 (m, 11, aromatics and NH), 8.03 (s, 3, CCH_3).

Anal. Calcd for $C_{15}H_{14}NSO_2Cl$: C, 58.52; H, 4.58. Found: C, 58.36; H, 4.71.

Cleavage of Sulfonamide 17 with Hydrogen Chloride. To 1.00 g of sulfonamide **17** was added 25 ml of chloroform that had been saturated with hydrogen chloride. The reaction was allowed to proceed at room temperature for 17 hr. A solid which precipitated was filtered, 0.30 g, mp 151–153°, which proved to be benzenesulfonamide by comparison with an authentic sample. The filtrate was treated with 10% KOH solution and extracted with ether. The ethereal solution was dried and removal of the ether gave 0.44 g of a pale yellow liquid which proved to be α-chloropropiophenone by comparison with an authentic sample.[30]

Attempted reaction of 2,3-diphenyl-1-azirine with benzenesulfonyl chloride in pyridine for 29 hr led to a quantitative recovery of 2,3-diphenyl-1-azirine (**9**).

The Attempted Reactions of Azirines 3 and 9 with Benzyl Chloride and Methyl Iodide. Azirines **3** and **9** were refluxed in acetone with either methyl iodide or benzyl chloride for periods up to 160 hr. Although some discoloration occurred, nmr analysis indicated that essentially no reaction had taken place.

Basicity of 3-Methyl-2-phenyl-1-azirine. Azirine **3** was insoluble in 10% HCl solution but rapidly turned orange.

To 1.00 g of the azirine was added 10 ml of 37% HCl solution. A colorless solution formed which was poured into 40 ml of 20% KOH solution and ice. This was extracted with ether. The ethereal extracts were combined and dried with magnesium sulfate. Removal of the solvent gave 1.01 g of a yellow solid which had the pungent odor of azirine **3**. Nmr analysis indicated the presence of azirine **3** by comparison of the integration of the methyl doublet of the azirine, τ 8.68, with that of the aromatic protons, τ 2.0–3.0.

Attempted Reaction of Chloroaziridine 6 with Sodium Hydride. To 0.10 g of sodium hydride which had been washed with pentane to remove the mineral oil was added 10 ml of dry 1,2-dimethoxyethane (DME). To this slurry was added 0.630 g of chloroaziridine **6** in 5 ml of DME. The reaction mixture was stirred for 18 hr, and the DME solution was separated from the salts. Removal of the ether gave a pale green oil which proved to be a quantitative recovery of the chloroaziridine **6** by comparison of its nmr spectrum with that of an authentic sample.

Attempted Reaction of Chloroaziridine 6 with 1,4-Diazabicyclo-[2.2.2]octane (DABCO). To 351 mg of DABCO was added 454 mg of chloroaziridine **6** and 15 ml of dry ether. The reaction stood at room temperature for 24 hr and removal of the ether with reduced pressure gave a quantitative recovery of the chloroaziridine **6** and DABCO by comparison of its nmr spectrum with that of an authentic sample of **6** and DABCO.

Determination of the Carbon-13–Hydrogen Coupling Constant for 2-Phenyl-1-azirine (19). The nmr spectrum was recorded using a Varian A-60 spectrometer on a neat sample of azirine **19**. The methylene protons occurred at τ 6.72 (external TMS). Several spinning frequencies were used in order to ascertain that the absorptions were not spinning side bands.

Acknowledgment. Support of this investigation by U. S. Public Health Service Grant CA-04474 from the National Cancer Institute is gratefully acknowledged.

(29) F. M. Campbell, B. F. Campbell, J. F. McKenna, and E. P. Chapun, *J. Org. Chem.*, **8**, 103 (1943).

(30) E. M. Kosower, W. J. Cole, G. S. Wu, D. E. Cardy, and G. Meisters, *ibid.*, **28**, 630 (1963).