Synthesis and Reactions of 1-Azirines[1a]

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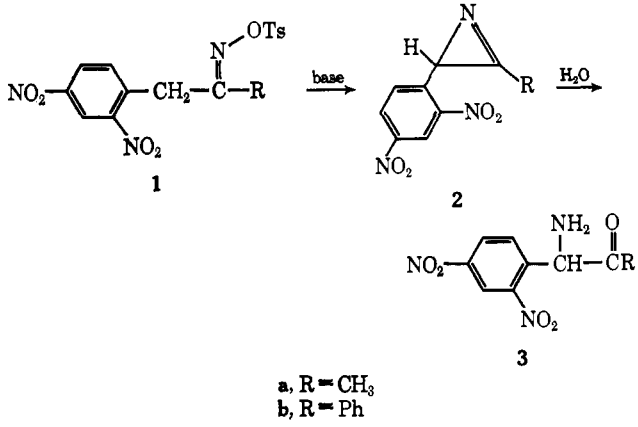
Abstract: A general synthesis of 1-azirines is described involving the photolysis of vinyl azides, which in turn can be readily obtained from the corresponding olefins. The photolysis usually proceeds in high yield and can also be applied to the synthesis of fused azirines. Infrared and nmr spectral properties as well as reactions of 1-azirines are discussed. Photolysis of vinyl azides in methanol containing sodium methoxide leads to amino ketals that provide a regiospecific synthesis of α-amino ketones. The ketals were shown to arise from the addition of methanol to the azirine followed by a ring opening of the 2-methoxyaziridine in methanol. Lithium aluminum hydride reduction of 1-azirines occurs in a stereospecific manner to give *cis*-2,3-disubstituted aziridines.

During his investigations of the reaction of oxime tosylates with base to give α-amino ketones, Neber isolated an intermediate to which he assigned the 1-azirine ring structure.[2] Since the incorporation of a double bond into an already highly strained three-membered ring was thought to preclude the very existence of the 1-azirine system, Neber's original assignment was seriously doubted. Hatch and Cram, after



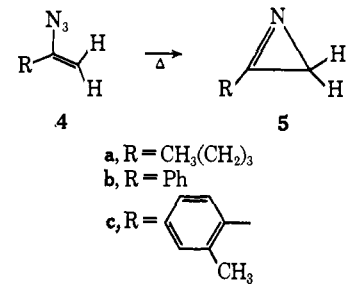
1 2 3

a, R = CH_3
b, R = Ph

an extensive study, confirmed the 1-azirine structure as the most plausible for Neber's intermediate.[3]

Although the Neber rearrangement generally does not lend itself for the synthesis of 1-azirines, a limited number of azirines have successfully been synthesized by a modified Neber reaction.[4] Very recently, the reaction of nitrile oxides with phosphonium ylides has been shown to lead to azirines.[5] The addition of dimethylsulfonium methylide to benzonitrile gave only a small amount of azirine in addition to other products.[6] The photolysis of isoxazoles to oxazoles has also led to the isolation of 1-azirines as intermediates.[7]

A synthesis of the 1-azirine ring system was developed by Smolinsky,[8] who discovered that the pyrolysis of vinyl azides yields 1-azirines. This method has been successful for the synthesis of three 1-azirines (**5a–c**). This



4 5

a, R = $CH_3(CH_2)_3$
b, R = Ph
c, R =

synthesis appears to be limited only to the availability of the prerequisite vinyl azide, which unfortunately, as Smolinsky states, "... can be a rather severe limitation."

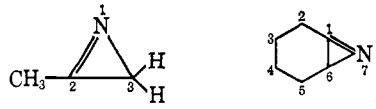
With the development of a general vinyl azide synthesis in our laboratories,[9] we initiated a study to test the generality of this reaction with respect to structural variations in the vinyl azide.

Since both photolysis and pyrolysis are known to induce loss of nitrogen in organic azides,[10] we decided to explore photolysis as a means of converting vinyl azides into 1-azirines. Photolysis is advantageous since a variety of solvents can be employed, and the reaction can be carried out at low temperatures. For example, the pyrolysis of 2-azido-1-hexene is reported to give considerable amounts of polymer[8] whereas we observed little polymerization when this azide was photolyzed.

Synthesis of 1-Azirines

By means of photolysis of vinyl azides we were successful in the synthesis of several (see Table I) 1-azirines including the first 1-azirines fused to other ring systems.

(1) (a) Stereochemistry. XXXII. For paper XXXI, see A. Hassner, J. M. Larkin, and J. E. Dowd, *J. Org. Chem.*, **33**, 1733 (1968); (b) NASA predoctoral fellow; (c) presented in part before the 153rd National Meeting of the American Chemical Society, Miami Beach, Fla., April 1967, Paper O-161. (d) 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-methylazirene, or 3-methyl-2H-azirine. Fused azirine ii would be 7-azabicyclo[4.1.0]hept-1(7)-ene.



i

ii

(2) P. W. Neber and A. Burgard, *Ann. Chem.*, **493**, 281 (1932).

(3) (a) M. J. Hatch and D. J. Cram, *J. Am. Chem. Soc.*, **75**, 33 (1953); (b) D. J. Cram and M. J. Hatch, *ibid.*, **75**, 38 (1953).

(4) (a) R. F. Parcell, *Chem. Ind.* (London), 1396 (1963); (b) D. F. Morrow, M. E. Butler, and E. C. Y. Huang, *J. Org. Chem.*, **30**, 579 (1965).

(5) (a) H. J. Bestman and Kunstmann, *Angew. Chem. Intern. Ed. Engl.*, **4**, 1039 (1966); (b) R. Huisgen and J. Wulff, *Tetrahedron Letters*, 917 (1967).

(6) H. Koenig, H. Metzger, and K. Seelert, *100 Jahre BASF, Aus. Forsch.*, 49 (1965); *Chem. Abstr.*, **64**, 17409*f* (1966).

(7) (a) E. F. Ullman and B. Singh, *J. Am. Chem. Soc.*, 88, 1844 (1966); (b) D. W. Kurtz and H. Shechter, *Chem. Commun.*, 689 (1966).

(8) G. Smolinsky, *J. Org. Chem.*, **27**, 3557 (1962).

(9) A. Hassner and F. W. Fowler, *ibid.*, in press.

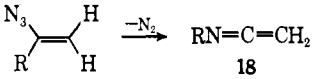
(10) R. A. Abramovitch and B. A. Davis, *Chem. Rev.*, **64**, 149 (1964).

Table I[a]

Compound	Crude yield, %	Bp, °C (mm), or mp, °C	Ir C=N absorption, cm^{-1}
3-Methyl-2-phenyl-1-azirine (**8**)	94	96 (15)	1740
2-Butyl-1-azirine (**9**)	81	80 (145)	1776
2-(β-Phenylethyl)-1-azirine (**10**)	93	108–110 (10)	1772
2-Phenyl-1-azirine (**11**)	94	83 (10)	1740
9-Azabicyclo[6.1.0]non-1(9)-ene (**12**)	93	76 (20)	1770
9-Azabicyclo[6.1.0]non-1(9),2-diene (**13**)	*b*	38 (0.20)	1740
2,3-Diethyl-1-azirine (**14**)	55	68 (130)	1778
2-Benzyl-1-azirine (**15**)	*b*	74 (1.5)	1780
3-Carbomethoxy-2-phenyl-1-azirine (**16**)	45	45–45.5	1773

[a] Glpc and spectral data of the crude azirines indicated that they generally were of greater than 90% purity. Distillation of the crude 1-azirines generally caused a decrease in yield of up to 30% due to polymerization. [b] Quantitative.

The pyrolysis of α-azidostyrene is reported to give a small amount of ketenimine in addition to 2-phenyl-1-azirine.[8] Ketenimines arise from the migration of the substituent geminal to the azido function similar to the well-known Curtius reaction.[11]



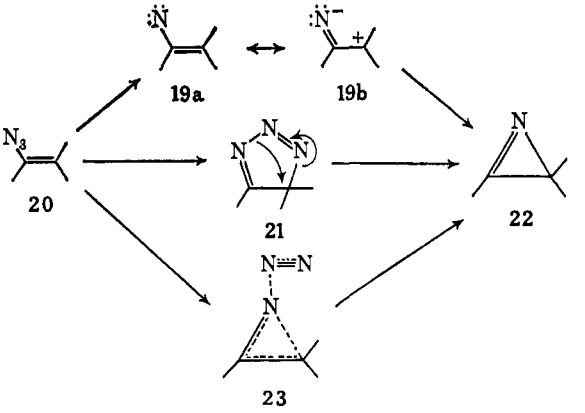
17 **18**

We observed no ketenimine when conjugated vinyl azides, such as α-azidostyrene, were photolyzed. This can be attributed to different mechanisms for photolysis and pyrolysis or to different energy states of the same intermediate. Evidently, the migratory aptitude of an alkyl group in the photolytic reaction is greater than that of phenyl.

Meek and Fowler[12] have observed that when β-azidovinyl *p*-tolyl sulfone was pyrolyzed, *p*-toluenesulfonylacetonitrile, by exclusive hydrogen migration, was the only product. However, the photolysis of this vinyl azide in wet solvents gave 2,3-di-*p*-toluenesulfonylaziridine which they have shown to arise from the addition of *p*-toluenesulfinic acid to the intermediate 1-azirine. Therefore, photolysis appears to be generally more selective for the formation of 1-azirines than is pyrolysis.

Three plausible mechanisms can be postulated for the photolysis of vinyl azides. One involves the loss of nitrogen from the vinyl azide to give the vinylnitrene **19**. This intermediate should be dipolar in nature. However, when α-azidostyrene was photolyzed in the presence of acetonitrile or phenylacetylene, known 1,3-dipolarophiles for carbethoxynitrene,[13] no products resulting from a dipolar addition were found. This cannot be regarded as evidence against a nitrene for it is possible that intramolecular ring closure is greatly preferred to dipolar addition for such an intermediate.

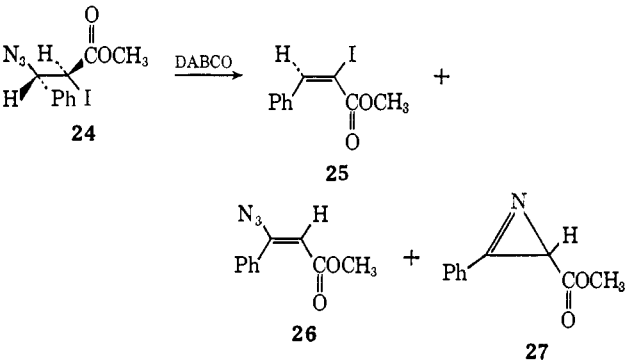
(11) P. A. S. Smith in "Molecular Rearrangements," P. de Mayo, Ed., John Wiley and Sons, Inc., New York, N. Y., 1963, Chapter 8.
(12) J. S. Meek and J. S. Fowler, *J. Am. Chem. Soc.*, **89**, 1967 (1967).
(13) W. Lwowski, A. Hartenstein, C. DeVita, and R. L. Smick, *Tetrahedron Letters*, 2497 (1964); R. Huisgen and H. Blashchke, *Ann.*, **586**, 145 (1965).



19a **19b** **20** **21** **22** **23**

For some vinyl azides, pyrolysis can be a convenient method of synthesis of 1-azirines. If the vinyl azide is substituted with two large *cis* substituents, then these azides lose nitrogen at a relatively low temperature to give 1-azirines.[14] In fact, that is the method of choice for the synthesis of 2,3-diphenyl-1-azirine (**53**) from *trans*-stilbene.[14a]

When iodo azide **24** was treated with 1,4-diazabicyclo[2.2.2]octane (DABCO) in acetone at room temperature a 1:2:3 mixture of methyl α-iodocinnamate (**25**), 3-carbomethoxy-2-phenyl-1-azirine (**27**), and methyl β-azidocinnamate (**26**) was produced. Although the vinyl azide **26** was never isolated its presence was inferred from the singlet absorption in the nmr spectrum (CCl_4) at τ 4.32 which disappeared on warming. Azirine formation was completely suppressed if the elimination was carried out at 5° and, in addition to some original iodo azide, only **25** and the vinyl azide were obtained.[9] Since the reaction is very slow at 5°, the elimination for preparative purposes was carried out at room temperature. Pyrolysis of the reaction mixture in refluxing Skellysolve B (bp 60–70°) allowed the conversion of the remaining vinyl azide **26** to azirine **27**. No isoxazole was found, as was the case when the IN_3 adduct to benzalacetophenone was treated with DABCO.[14a] This is consistent with the decreased basicity of the carbonyl oxygen in **26** as compared to the corresponding keto vinyl azide from benzalacetophenone.



24 **25** **26** **27**

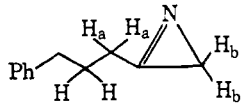
Elimination of hydrogen azide producing **25** was probably facilitated in this case because of the greater acidity of the proton α to the carbonyl function. We have previously observed that if the elimination was carried out using potassium hydroxide in methanol,

(14) (a) F. W. Fowler, A. Hassner, and L. A. Levy, *J. Am. Chem. Soc.*, **89**, 2077 (1967); (b) R. J. Isbister, unpublished results, University of Colorado, 1967.

elimination of both hydrogen iodide and hydrogen azide took place and only phenylpropiolic acid was isolated.[14a]

The C=N stretching frequency in 3-alkyl-substituted azirines generally occurs near 1775 cm^{-1} (see Table I) reflecting the highly strained ring system. A 3-phenyl substituent lowers the absorption to 1740 cm^{-1} due to conjugation. Azirine **27** has its infrared imine absorption at 1773 cm^{-1}. Since this is a conjugated 1-azirine, this absorption would appear to be anomalous. However, the carbomethoxy substituent is electron withdrawing, and it is known that ketones possessing electronegative substituents such as halogens at the α position have their carbonyl absorptions shifted to higher energy.[15]

The nmr spectra of 1-azirine derivatives are very revealing of the electronic nature of this small, highly strained ring system. The exocyclic methylene protons (H_a) α to the imine bond in azirine **28** have their nmr absorption at τ 7.04. However, the methylene ring protons (H_b), which are not only α to the imine but are also α to a nitrogen substituent, are found upfield at τ 8.80. This shielding of hydrogen nuclei attached to



28

three-membered rings is well known and has been attributed to ring currents in these small rings.[16] We have also observed that the ring protons of azirines absorb at a slightly higher field than those of the corresponding aziridines in spite of the presence of unsaturation in the ring. For example, the absorption of the ring proton for 3-methyl-2-phenyl-1-azirine (**8**) occurs at τ 7.76 whereas that of the corresponding aziridine is at 7.58. As expected, the azirine ring protons occur at higher field in 2-alkyl- than in the conjugated 2-phenylazirines (*e.g.*, τ 8.16 in **14** *vs.* 7.76 in **8** and τ 8.8 in **10** *vs.* 8.3 in **11**).

The ^{13}C–H coupling constant[17] of 2-phenyl-1-azirine (**11**) indicates 35.6% s character for the exocyclic orbitals of this azirine compared to 32.2% for ethylenimine.[18] This change in hybridization results in a large bond angle for exocyclic substituents of 1-azirines and consequently explains the observed upfield shift of the ring proton in 1-azirine as compared to the corresponding aziridine. The effect places the ring proton further in the shielding cone of the three-membered ring and possibly into the shielding cone of the imine bond.

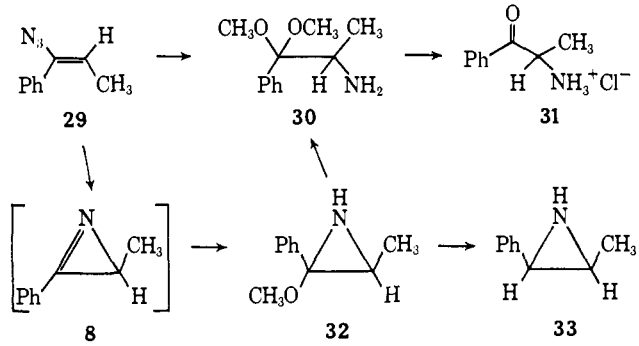
A plausible alternative explanation, suggested previously,[19] is that there is a larger ring current in 1-azirines than in aziridines.

All liquid 1-azirines which we have synthesized have very unpleasant characteristic odors and are somewhat irritating to the skin. The conjugated 2,3-disubstituted 1-azirines are quite stable if stored under argon or nitrogen below 0°. 2,3-Diphenyl-1-azirine (**53**) is a solid. 1-Azirines substituted only by an alkyl group at the 2 position are relatively unstable. In fact, 2-benzyl-1-azirine (**15**) on exposure to the atmosphere rapidly turns brown within minutes and even at *ca.* 10° under argon polymerizes completely within a few days.

Synthesis of Amino Ketones

Since hydrolysis of 1-azirines produces amino ketones, our method also allows for a regiospecific[20] synthesis of amino ketones from olefins. However, if the amino ketone is the desired product, higher yields are obtained if a slightly modified procedure is used.

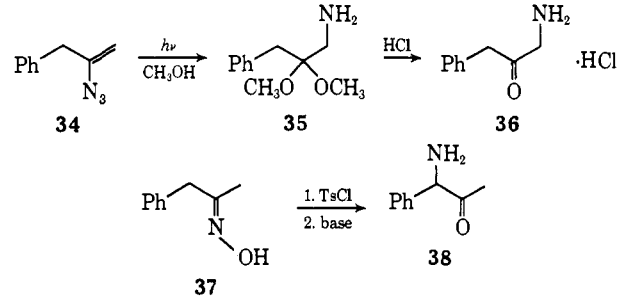
Photolysis of the vinyl azide in methanol containing 0.5% sodium methoxide rather than in an inert solvent gave directly the amino ketone dimethyl ketal. These ketals are usually not isolated but are hydrolyzed directly to the amino ketone hydrochlorides with aqueous hydrochloric acid. Methoxyaziridine **32** was the anticipated product. However, this is apparently unstable under the reaction conditions. The methoxyaziridine **32** was prepared by the addition of methanol to azirine **8** and its structure proven by reduction to 2-methyl-3-phenylaziridine (**33**).[3b] Further treatment of the methoxyaziridine **32** with methanol results in



29 **30** **31** **8** **32** **33**

ring opening to give ketal **30**, thus providing evidence for the pathway as outlined.

The above method compliments Neber's synthesis of amino ketones. For example, allylbenzene led to the amino ketone **36** whereas oxime **37** when subjected to the Neber reaction[21] gave its isomer **38**.



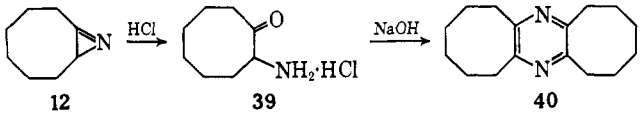
34 **35** **36** **37** **38**

Fused and 2-Monosubstituted 1-Azirines

It was of interest to establish whether azirines fused to other ring systems could be synthesized. To minimize strain in these bicyclic systems we chose the eight-

(15) R. N. Jones and C. Sandorfy in "Technique of Organic Chemistry," Vol. IX, W. West, Ed., Interscience Publishers, Inc., New York, N. Y., 1956, p 474.
(16) J. D. Roberts, *Angew. Chem. Intern. Ed. Engl.*, **2**, 53 (1963).
(17) F. W. Fowler and A. Hassner, *J. Am. Chem. Soc.*, **90**, 2875 (1968).
(18) F. S. Mortimer, *J. Mol. Spectry.*, **5**, 199 (1960).
(19) G. R. Harvey and K. W. Ratts, *J. Org. Chem.*, **31**, 3907 (1966).
(20) We have proposed the term *regiospecific* to indicate specificity in orientation or direction in organic reactions: A. Hassner and F. Boerwinkle, *J. Am. Chem. Soc.*, **90**, 216 (1968); A. Hassner, *J. Org. Chem.*, **33**, 1733 (1968).
(21) C. O'Brien, *Chem. Rev.*, **64**, 81 (1964).

membered vinyl azides as starting materials. Photolysis of 1-azidocyclooctene and 2-azidocycloocta-1,3-diene gave in over 90% yield the fused azirines **12** and **13**, respectively. The synthesis of **12** and **13** represents the first examples of fused 1-azirines. Azirine **12** is relatively stable and displays no unusual properties that would indicate an unstable ring system. It can be readily hydrolyzed to the amino ketone, which when treated with base dimerizes to the pyrazine **40**.

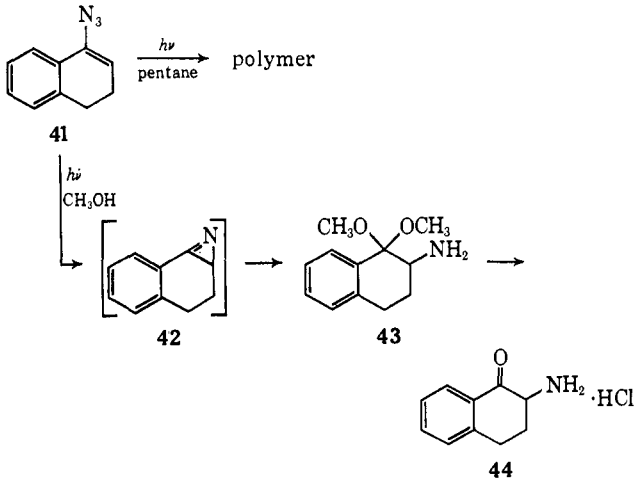


12 **39** **40**

The carbon–nitrogen double bond stretching frequency of **12** occurs at 1770 cm^{-1} and is that expected for nonconjugated azirines. The appearance of the carbon–nitrogen double bond at 1740 cm^{-1} in **13** demonstrates that conjugation of the imine with a double bond results in lowering of the energy of absorption.

We next investigated the possibility of obtaining azirines fused to smaller rings.

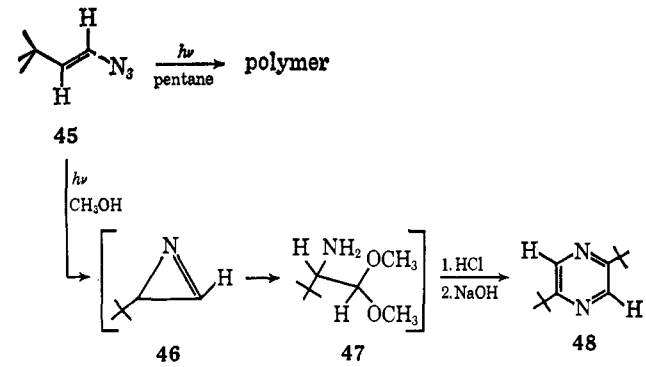
Photolysis of **41** resulted only in unreacted vinyl azide and a large amount of polymeric material which inhibited further photolysis. It is possible that the polymeric material was due either to the polymerization of the vinyl azide or to the polymerization of the highly strained 1-azirine. To differentiate between these two alternatives we carried out the photolysis in methanol containing 0.5% sodium methoxide with the hope of trapping the 1-azirine if formed. This was a successful experiment and hydrolysis of the intermediate ketal **43** produced a good yield of the amino ketone **44**.



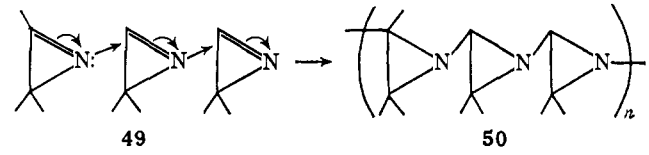
41 **42** **43** **44**

Apparently, the fused azirine **42** was being formed in inert solvents but, due to increased ring strain, it polymerized rapidly.

We have previously reported that iodine azide adds in a regiospecific manner to *t*-butylethylene giving 1-azido-2-iodo-3,3-dimethylbutane.[14a] Elimination of hydrogen iodide gave cleanly the vinyl azide **45**. This vinyl azide possesses the potential for becoming the first reported 3-monosubstituted 1-azirine. Unfortunately, photolysis of **45** in inert solvents gave only polymeric material and a trace of a compound identified as 2,5-di-*t*-butylpyrazine (**48**). If the reaction was carried out in methanol, a good yield of pyrazine **48** was obtained upon work-up with acid, presumably *via* **46** and **47**. Although the structure of the azirine polymer is unknown, it probably results from the addition of the lone pair of one azirine to the imine linkage of another, etc. If the 1-azirine is substituted at the 2 position, then this type of polymerization is sterically inhibited. However, if the 1-azirine is substituted only at the 3 position, there is little steric inhibition toward polymerization.



45 **46** **47** **48**

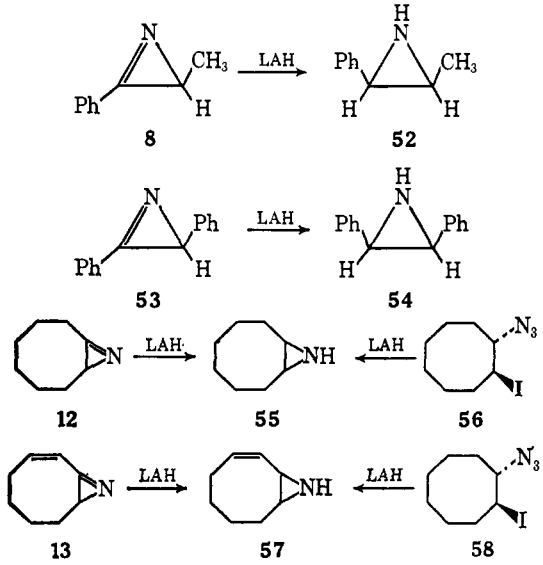


49 **50**

Reduction of 1-Azirines

Hatch and Cram found that 1-azirines can be reduced with lithium aluminum hydride[3] but the reported yield, less than 1%, would indicate this to be a very poor reaction and of no synthetic value. We have discovered that with simple azirines this is not only a good aziridine synthesis but is also a highly stereospecific reaction. For instance, reduction of **8** and **53** gave in high yield *cis*-aziridines **52** and **54**, respectively.

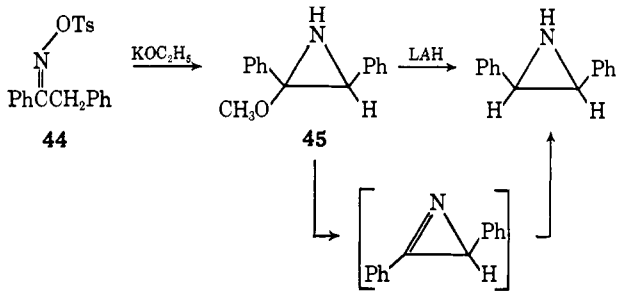
This high stereospecificity is also consistent with a large exocyclic dihedral angle of the saturated carbon atom in azirines **8** and **53**. This causes the imine bond to be preferentially shielded by the R group and allows for the approach of lithium aluminum hydride to occur only from the less hindered side of the molecule. Fused azirines **12** and **13** could likewise be reduced by lithium aluminum hydride in good yield to the corresponding aziridines. Aziridines **55** and **57** were independently



8 **52** **53** **54** **12** **55** **56** **13** **57** **58**

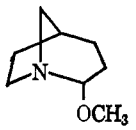
synthesized by reduction of β-iodo azides **56** and **58**, respectively.[22a]

Cram and Hatch have observed that 2-methoxy-2,3-diphenylaziridine (**45**) of unspecified stereochemistry was reduced with lithium aluminum hydride to *cis*-2,3-diphenylaziridine.[3b] Methoxyaziridine **45** was presumably produced in the Neber reaction by the addition



44 **45** **53**

of methanol across the carbon–nitrogen double bond of the azirine and most likely consisted of a mixture of *cis* and *trans* or mainly *cis*-methoxyaziridine. If the latter is the case direct displacement of the methoxyl group by hydride must have occurred with retention of configuration in order to produce the *cis*-aziridine. A more logical explanation appears to us to be that lithium aluminum hydride first eliminates methanol to give the azirine **53** which, as we now known, is stereospecifically reduced to *cis*-2,3-diphenylaziridine. Support of this view is provided by the reported elimination of alcohol from an alkoxyaziridine[4a] and by the stability of **59** toward lithium aluminum hydride.[22b] In **59** formation of an imino linkage would be in violation of Bredt's rule.



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Experimental Section[23]

General Procedure for the Conversion of Vinyl Azides to 1-Azirines by Photolysis. The source for ultraviolet radiation in all cases was the Srinivasan–Griffin Rayonet photochemical reactor equipped with the "black light" phosphor lamps.[24] Using a quartz flask, the vinyl azide was dissolved in either cyclohexane or pentane (previously distilled from calcium hydride) to make a 5% (w/v) solution. The reaction (protected from atmospheric moisture) was then placed in the photoreactor and, if pentane was used, a reflux condenser was attached. The photolyses were discontinued when there was no azide remaining as indicated by the disappearance of the strong absorption at *ca.* 2100 cm^{-1} in the infrared spectrum. The small amount of polymer was filtered. The solvent was then removed with reduced pressure (protected from moisture) with slight heating if cyclohexane was used as a solvent. The crude 1-azirine is obtained usually as a pale yellow liquid and if further purification is necessary, it can be distilled at reduced pressure. If it is essential that the ketenimine be removed, a very efficient column is needed, since the azirine and ketenimine have very similar boiling points. The ketenimine, having a very strong infrared absorption at *ca.* 2080 cm^{-1}, is present in less than 10% of the total photolysate.

3-Methyl-2-phenyl-1-azirine (8) was prepared by photolysis in cyclohexane from 1-phenyl-1-azido-1-propene[9] in 94% yield. Distillation produced the analytical sample: bp 96° (15 mm); nmr (CCl_4) τ 2.0–3.0 (m, 5, aromatic protons), 7.74 (q, 1, J = 5 Hz, $CHCH_3$), and 8.68 (d, 3, J = 5 Hz, $CHCH_3$); ir (neat) 1740 cm^{-1} (C=N).

Anal. Calcd for C_9H_9N: C, 82.40; H, 6.92. Found: C, 82.24; H, 7.13.

2-Butyl-1-azirine (9) was prepared in pentane by photolysis from 2-azido-1-hexene[9] in 81% yield. The pure azirine was obtained by distillation through a 12-in., spinning-band column: bp 80° (145 mm) (lit.[8] 57° (54 mm)); nmr (CCl_4) τ 7.22 (t, broad, 2, J = *ca.* 7 Hz), 8.0–9.2 (m, 9); ir (neat) 1776 cm^{-1} (C=N) (lit.[7] 1773 cm^{-1} (CCl_4)).

2-(β-Phenylethyl)-1-azirine (10) was prepared in pentane by photolysis from 2-azido-4-phenyl-1-butene[9] in 93% yield. Distillation through a 12-in., spinning-band column produced the analytical sample: bp 108–110° (10 mm); nmr ($CDCl_3$) τ 2.75 (s, 5, aromatic protons), 7.04 (s, 4, CH_2CH_2), and 8.80 (s, 2, ring protons); ir (neat) 1772 cm^{-1} (C=N).

Anal. Calcd for $C_{10}H_{11}N$: C, 82.72; H, 7.64. Found: C, 82.97; H, 7.84.

2-Phenyl-1-azirine (11) was prepared in pentane by photolysis from α-azidostyrene[9] in 94% yield. A pure sample of the azirine was obtained by distillation through a 12-in., spinning-band column: bp 83° (10 mm) (lit.[8] 80° (10 mm)); nmr (CCl_4) τ 2.0–2.8 (m, 5, aromatic protons) and 8.27 (s, 2 ring protons); ir (neat) 1740 cm^{-1} (C=N) (lit.[8] 1742 cm^{-1} (CCl_4)). The carbon-13–hydrogen coupling constant was determined on the neat liquid at several spinning speeds in order to eliminate spinning side bands ($J_{^{13}C-H}$ = 178 Hz).

9-Azabicyclo[6.1.0]non-1(9)-ene (12) was prepared by photolysis in pentane from 1-azidocyclooctene[9] in 93% yield. Distillation through a 12-in., spinning-band column produced the analytical sample: bp 76° (20 mm); nmr (CCl_4) τ 7.1–7.5 (m, 2) and 7.8–9.5 (m, 11); ir (neat) 1770 cm^{-1} (C=N).

Anal. Calcd for $C_8H_{13}N$: C, 79.29; H, 9.15. Found: C, 79.08; H, 9.03.

9-Azabicyclo[6.1.0]nona-1(9),2-diene (13) was prepared by photolysis in pentane from 2-azido-1,3-cyclooctadiene[9] in quantitative yield. Distillation through a 12-in., spinning-band column produced the analytical sample: bp 38° (0.20 mm); nmr (CCl_4) τ 3.0–3.6 (m, 2, vinylic protons) and 6.6–9.3 (m, 9); ir (neat) 1610 (C=C) and 1740 cm^{-1} (C=N).

Anal. Calcd for $C_8H_{11}N$: C, 79.29; H, 9.15. Found: C, 79.08; H, 9.03.

2,3-Diethyl-1-azirine (14) was prepared by photolysis in pentane from 3-azido-3-hexene[9] in 55% yield. Distillation through a 12-in., spinning-band column produced the analytical sample: bp 68° (130 mm); nmr (CCl_4) τ 7.23 (q, 2, J = 7.5 Hz), 8.16 (t, 1, J = 4 Hz), and 8.4–9.3 (m, 8); ir (neat) 1773 cm^{-1} (C=N).

Anal. Calcd for $C_8H_{11}N$: C, 74.17; H, 11.41. Found: C, 74.14; H, 11.52.

2-Benzyl-1-azirine (15) was prepared by photolysis in cyclohexane from 2-azido-3-phenyl-1-propene[9] in quantitative yield. Distillation through a 12-in., spinning-band column produced the analytical sample: bp 74° (1.5 mm); nmr ($CDCl_3$) τ 2.75 (s, 5, aromatic protons), 5.98 (s, 2, $-CH_2-$), and 8.63 (s, 2, ring protons); ir (neat) 1785 cm^{-1} (C=N).

Anal. Calcd for C_9H_9N: C, 82.46; H, 6.92. Found: C, 81.67; H, 7.07.

3-Carbomethoxy-2-phenyl-1-azirine (16) and Methyl α-Iodocinnamate (25). To 30.0 g of the iodo azide **24** was added 150 ml of acetone and 17.0 g of DABCO. The mixture stood at room temperature for 21.5 hr. To the now yellow reaction mixture was added 1.5 l. of water, and the reaction mixture was extracted with ether. The ethereal solution was washed with 5% HCl solution and then several times with cold water. The ethereal solution was then dried with $MgSO_4$. Removal of the ether at reduced pressure produced 15.0 g of an orange liquid. The nmr spectrum ($CDCl_3$) showed this to be a 1:2:3 mixture of methyl α-iodocinnamate, 3-carbomethoxy-2-phenyl-1-azirine, and presumably methyl *cis*-β-azidocinnamate[9] (see Discussion).

To 15.0 g of the above product was added 300 ml of Skellysolve B (bp 60–70°), and the mixture was refluxed for 3.5 hr. Removal of the solvent with reduced pressure and slight heating produced an orange oil which was distilled. The fraction boiling at 100–105°

(22) (a) G. J. Matthews and F. W. Fowler, unpublished data. (b) Private communication from Professor P. G. Gassman, The Ohio State University.

(23) 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 taken with either a Varian A-60 or A-60A spectrometer. Microanalysis were performed by either A. Bernhardt, Mulheim, Germany, or Gailbraith Laboratories, Knoxville, Tenn. In nmr descriptions, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet.

(24) Purchased from the Southern N. E. Ultraviolet Co., Middletown, Conn.

(0.3 mm) gave 10.30 g of a pale yellow oil. The nmr spectrum showed the distillate to be a 4:1 mixture of 2-carbomethoxy-3-phenyl-1-azirine and methyl α-iodocinnamate. The addition of *ca.* 200 ml of pentane followed by cooling to −20° produced 7.30 g of pale yellow crystals, mp 42–44°. Recrystallization from ethyl acetate and Skellysolve B (bp 60–70°) gave the analytical sample: mp 45–45.5°; nmr ($CDCl_3$) τ 2.0–2.5 (m, 5, aromatic protons), 6.25 (s, 3, OCH_3), and 7.15 (s, 1, ring proton); ir (KBr) 1770 cm^{-1} (C=N).

Anal. Calcd for $C_{10}H_9O_2N$: C, 68.56; H, 5.18. Found: C, 68.82; H, 5.39.

Removal of the pentane from the above filtrate produced 2.96 g of a yellow liquid which proved to be methyl α-iodocinnamate (**25**). This liquid could be further purified by passing it through 80 g of Merck No. 71707 aluminum oxide with a 1:1 mixture of pentane and methylene chloride giving 2.45 g of pure methyl α-iodocinnamate: nmr (CCl_4) τ 1.80 (s, 1, CH=C), 2.2–2.8 (m, 5, aromatic protons), and 6.21 (s, 3, OCH_3); the ir spectrum shows no azide absorption.

The structure of methyl α-iodocinnamate (**25**) was confirmed by conversion to phenylpropiolic acid.[14a] To 583 mg of methyl α-iodocinnamate was added 6.0 g of potassium hydroxide in 20 ml of methanol. The reaction mixture stood at room temperature for 15 hr and then the methanol was removed to give 339 mg of pale yellow crystals. Recrystallization from benzene and cyclohexane gave a pure sample of phenylpropiolic acid, mp 134–136° (lit.[25] 135–136°). The infrared spectrum was identical with that of an authentic sample.

Photolysis of *cis*-1-Azido-1-phenyl-1-propene in Methanol Containing 0.5% Sodium Methoxide. To 4.00 g of *cis*-1-azido-1-phenyl-1-propene[9] was added 80 ml of anhydrous methanol and 0.400 g of sodium methoxide. The reaction mixture was photolyzed for 18 hr during which time the solution went from pale yellow to colorless. The solvent was removed at reduced pressure to give a pale yellow paste. This was treated with ether and washed with water. The ethereal solution was dried with $MgSO_4$ and then removed at reduced pressure giving 1,1-dimethoxy-1-phenyl-2-aminopropane (**30**) as a pale yellow liquid: nmr ($CDCl_3$) τ 2.4–2.8 (m, 5, aromatic protons), 6.5–6.9 (multiplet with a sharp singlet at 6.76, seven protons), 8.92 (broad singlet, two protons, NH_2), and 9.15 (d, 3, J = 6.5 Hz, $CHCH_3$).

The phenylcarbamoyl derivative was prepared from phenyl isocyanate in Skellysolve B (bp 60–70°) and was recrystallized from methanol–ethyl acetate, mp 226–228°.

Anal. Calcd for $C_{18}H_{22}N_2O_3$: C, 68.77; H, 7.05. Found: C, 68.55; H, 6.99.

Acid Hydrolysis of 1,1-Dimethoxy-1-phenyl-2-aminopropane (30). To 3.15 g of **30** was added 50 ml of methanol and 10 ml of a 20% HCl solution. The reaction was refluxed for 4 hr and then the solvent was removed giving a brown semisolid. Recrystallization from methanol–ethyl acetate gave 1.96 g of colorless crystals of α-aminopropiophenone hydrochloride (**31**): mp 193–195° (lit.[26] 182°).

The benzamide derivative was prepared from benzoyl chloride in pyridine: mp 103–104° (lit.[27] 104–105°).

Addition of Methanol to 3-Methyl-2-phenyl-1-azirine (8). To 0.650 g of 3-methyl-2-phenyl-1-azirine was added 20 ml of absolute methanol and 0.200 g of sodium methoxide. The reaction mixture became warm and turned yellow. After being allowed to stand at room temperature for 15 min, the solvent was removed at reduced pressure giving a yellow semisolid. This was treated with ether and was washed with water. The ethereal solution was dried with $MgSO_4$, and the solvent was removed giving 0.716 g of the methoxyaziridine **32**. The nmr spectrum ($CDCl_3$) showed τ 6.83, three-proton singlet absorption (OCH_3).

A similar reaction mixture was allowed to stand at room temperature for 14 hr. The nmr spectrum of the crude product showed two equal methoxy singlet absorptions at τ 6.83 (2-phenyl-2-methoxy-3-methylaziridine (**32**)) and 6.76 (1,1-dimethoxy-1-phenyl-2-aminopropane (**30**)). Refluxing this crude product in methanol containing 1% sodium methoxide caused the disappearance of the τ 6.83 absorption and an increase in the intensity of the 6.76 absorption.

Reduction of 2-Methoxy-2-phenyl-3-methylaziridine (32). To 1.31 g of 3-methyl-2-phenyl-1-azirine (**8**) was added 25 ml of absolute methanol and 0.250 g of sodium methoxide. The reaction mixture became warm and turned yellow. The solvent was removed at reduced pressure to give a yellow liquid. This liquid was treated with ether and washed with water. The ethereal solution was dried with $MgSO_4$. This ethereal solution of 2-methoxy-2-phenyl-3-methylaziridine was then added cautiously to 1.00 g of $LiAlH_4$ in 60 ml of absolute ether, and the reaction mixture was stirred at room temperature for 12 hr. The excess $LiAlH_4$ was decomposed with 5 ml of a 20% NaOH solution, and the inorganic salts were filtered. The ethereal filtrate was dried and the solvent removed at reduced pressure to give 1.19 g of a yellow liquid. The addition of pentane–ether followed by cooling produced a colorless solid. This was filtered giving 0.198 g of colorless crystals, mp 89–97°, which appeared to be 1-hydroxy-1-phenyl-2-aminopropane. Recrystallization from benzene raised the melting point to 98–100° (lit.[28] 103–105°). Removal of the solvent from the above filtrate produced 0.741 g of **33** as a yellow oil which crystallized when treated with pentane, mp 39–40° (lit.[29] 41–43°). The nmr spectrum was identical with that of an authentic sample of **33** prepared by the reduction of 3-methyl-2-phenyl-1-azirine with $LiAlH_4$.

1-Amino-3-phenyl-2-propanone Hydrochloride (36). To 4.00 g of 2-azido-3-phenyl-1-propene (**34**)[6] was added 20 ml of 2% sodium methoxide solution and 60 ml of absolute methanol. The solution was photolyzed for 24 hr, and removal of the solvent gave a colorless oil. Then *ca.* 200 ml of ether was added, and this was washed with water (three 100-ml portions). The ethereal layer was dried and the solvent removed to give 3.43 g of a yellow liquid. To 2.87 g of this yellow liquid was added 35 ml of methanol and 15 ml of a 20% HCl solution. The reaction was refluxed for 3 hr. Removal of the solvent gave a tan semisolid which was recrystallized from methanol–ethyl acetate giving 1.34 g of tan crystals, mp 210–212° dec. After several recrystallizations from methanol–ethyl acetate the melting point was 210–212° (lit.[30] 222.8–224°).

The benzamide derivative was prepared from benzoyl chloride in pyridine: mp 99.5–100° (from ethyl acetate); nmr ($CDCl_3$) τ 2.0–3.2 (m, 11, aromatic protons and NH), 5.66 (d, 2, J = 4.5 Hz, $NHCH_2$), and 6.22 (s, 2, benzylic protons).

Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97. Found: C, 75.69; H, 6.01.

2-Aminocyclooctanone Hydrochloride (39). To 1.23 g of azirine **12** was added 15 ml of methanol and 5 ml of a 10% HCl solution. The reaction was refluxed for 5.25 hr. The solvent was then removed with reduced pressure and heating to give 2.26 g of a tan solid, mp 195–198° (inserted 150°). Recrystallization from methanol and ethyl acetate gave the analytical sample, mp 202–203°.

Anal. Calcd for $C_8H_{17}NOCl$: C, 54.39; H, 8.56. Found: C, 54.60; H, 8.67.

Pyrazine 40. To 606 mg of 2-aminocyclooctanone hydrochloride (**39**) was added *ca.* 15 ml of 5% KOH solution. The initially clear solution slowly turned cloudy. The mixture was allowed to stand at room temperature for 2 days during which time a yellow solid precipitated. This solid was collected and dried giving 386 mg of yellow crystals, mp 102–105°. Recrystallization from Skellysolve B (bp 60–70°) gave the analytical sample: mp, 115–116° subl; the ir (KBr) spectrum showed no NH or C=O absorptions.

Anal. Calcd for $C_{16}H_{24}N_2$: C, 78.63; H, 9.90. Found: C, 78.45; H, 9.74.

2-Amino-1-tetralone Hydrochloride (44). To 4.00 g of 4-azido-1,2-dihydronaphthalene[9] was added 20 ml of a 2% sodium methoxide solution and 60 ml of absolute methanol. The reaction mixture was photolyzed for 16 hr. The solvent was removed from the dark green solution with reduced pressure and slight heating to give a red-brown semisolid. Ether (*ca.* 125 ml) was added to this solid, and the residual methanol and sodium methoxide were washed out with water (three 100-ml portions). The ether was dried and removed to give 3.28 g of a red oil. To 2.52 g of this red oil was added 40 ml of methanol and 15 ml of 20% HCl solution. The reaction mixture was refluxed for 2.75 hr, and the solvent was removed with reduced pressure and heating to give a brown residue. This residue was recrystallized once from methanol–methyl acetate to give 1.47 g of tan crystals, mp 196–200° dec (lit.[31] 201–202°).

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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]

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

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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-