(4) E. Spath and N. Pfaizer, *Chem. Ber.*, **68**, 2221 (1935).
(5) P. Carabateas and L. Harris, *J. Med. Chem.*, **9**, 6 (1966).
(6) E. Ziegler, W. Steiger, and T. Kappe, *Monatsh. Chem.*, **99**, 1499 (1968).
(7) G. E. Hardtmann, G. Koletar, O. R. Pfister, J. H. Gogerty, and L. Iorio, *J. Med. Chem.*, **18**, 447 (1975).
(8) G. E. Hardtmann, B. Huegi, J. H. Gogerty, L. C. Iorio, and H. W. Barnes, *J. Med. Chem.*, **14**, 878 (1971).
(9) L. J. Bellamy, "The Infra-red Spectra of Complex Molecules", 2nd ed, Wiley, New York, N.Y., 1958, p. 268.
(10) For example, K. K. Balasubramanian and B. Venugopalan, *Tetrahedron Lett.*, 2643 (1974); Castaigne, J. P. Maffrand, G. Ferrand, F. Eloy, and F. Toulouse, *Eur. J. Med. Chem.*, **9**, 539 (1974).
(11) R. P. Staiger and E. B. Miller, *J. Org. Chem.*, **24**, 1214 (1959).
(12) E. Ziegler, R. Wolf, and T. Kappe, *Monatsh. Chem.*, **96**, 418 (1965).
(13) For the preparation of the isatoic anhydrides utilized in this publication: G. E. Hardtmann, G. Koletar, and O. R. Pfister, *J. Hererocycl. Chem.*, **12**, 565 (1975).
(14) No attempts were made to optimize yields of the reactions.
(15) Prepared in 93% yield by the alkylation of 2-thio-1-(α,α,α-trifluoro-*o*-tolyl)urea [F. Kurzer and J. Canell, *Tetrahedron*, **19**, 1603 (1963)] with methyl iodide in ethanol. The material was used without further purification.
(16) W. G. Finnegan, R. A. Henry, and E. Lieber, *J. Org. Chem.*, **18**, 779 (1953).
(17) I. Ugi, U. Fetzer, U. Eholzer, H. Knupfer, and K. Offermann, *Angew. Chem.*, **77**, 492 (1965).

Thermal Decomposition of 2*H*-Azirines. Formation of Products Resulting from Carbon–Carbon Bond Cleavage[1]

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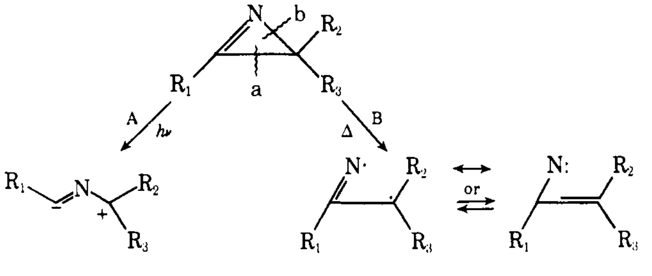
The synthesis and thermal decomposition of 2-methyl-3-phenyl- (**19a**), 2-ethyl-3-phenyl- (**19b**), 2,2-dimethyl-3-phenyl- (**19c**), and 2,3-dimethyl-2-phenyl-2*H*-azirines (**19d**) is described. Previously, products formed on thermal decomposition of 2*H*-azirines have been derived from initial C–N bond cleavage; in contrast, the products observed on heating **19a–c** (styrenes, benzonitrile, and HCN or acetonitrile) are formed by C–C cleavage, leading initially to iminocarbene intermediates. Evidence is presented that the primary mode of product formation from such an intermediate is 1,4-hydrogen shift, giving a 2-azabutadiene. The azabutadiene then fragments (via a small equilibrium concentration of substituted 1-azacyclobutene) leading to the final products. At higher temperatures, the azabutadienes are converted to dihydroisoquinolines as well.

Photochemical and thermal bond cleavage preferences in 2*H*-azirines appear to be quite distinct. Products formed during photochemical isomerizations appear to always involve carbon–carbon bond cleavage (path A, Scheme I), while thermal isomerization products arise from initial carbon–nitrogen bond cleavage (path B, Scheme I).

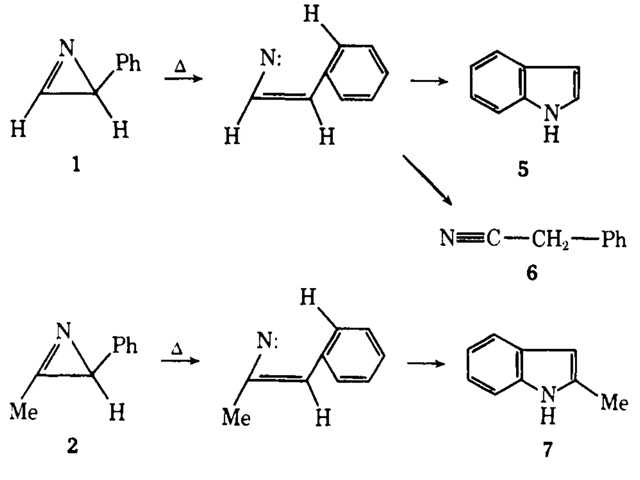
Scheme I



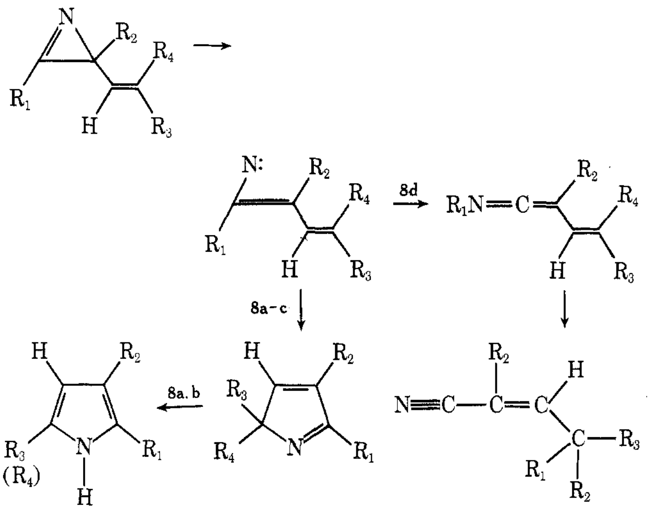
Azirine photochemistry has been extensively investigated by several groups. Padwa[3] and Schmid,[4] for example, have shown in independent studies that upon photolysis 3-phenyl-2*H*-azirines undergo cycloadditions with a variety of 1,3-dipolarophiles. These reactions apparently all proceed by initial C–C cleavage in the azirines, leading to dipolar species. Schmid and co-workers have also photolyzed triphenyl-2*H*-azirine in a 2,2-dimethylbutane–pentane matrix at −185 °C and observed a new uv maximum at ca. 350 nm (ε ~10^4). The authors assigned this band to a nitrile ylide species. They further showed that the ylide rearranged to starting azirine only photochemically, and were able to trap it at low temperatures using methyl trifluroacetate. Recent ab initio MO calculations by Salem,[5] utilizing a configuration interaction treatment, suggest that upon cleaving a C–C azirine bond, the ground state nitrile ylide energy surface is best reached by internal conversion from a singlet n,π* state at a C–N–C bond angle of 100°. Salem's calculations also predict a large barrier for thermal conversion of the ylide to azirine, but suggest a facile photochemical conversion.

Relative to the well-defined photochemistry of 2*H*-azirines, their thermal behavior is not as well understood. The first report of a 2*H*-azirine pyrolysis was made by Isomura and co-workers in 1968.[6] These workers prepared 2-phenyl-2*H*-azirine (**1**) and 3-methyl-2-phenyl-2*H*-azirine (**2**) by photolytic and thermal decomposition of *cis*- and *trans*-1-azido-2-phenylethene (**3c** and **3t**) and *cis*- and *trans*-2-azido-1-phenylpropene (**4c** and **4t**), respectively. Thermal decomposition of **1** in boiling hexadecane yielded a 1:1 mixture of indole (**5**) and phenylacetonitrile (**6**) in 86% isolated yield. Similar treatment of **2** gave only 2-methylindole (**7**). The most obvious mechanism for formation of **5**, **6**, and **7** involved a vinyl nitrene intermediate generated by rupture of the *carbon–nitrogen* bond, followed by insertion into the phenyl group or α-carbon–hydrogen bond (see Scheme II).

Scheme II



Scheme III

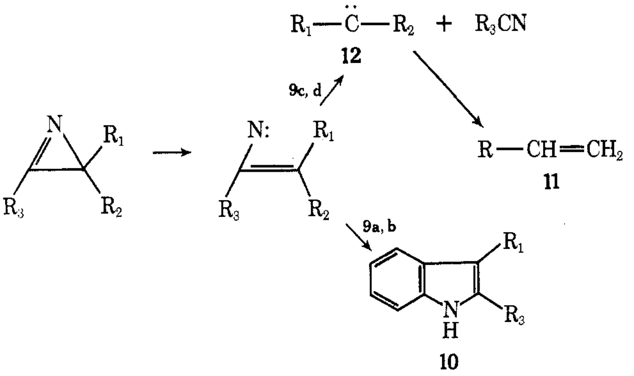


	R_1	R_2	R_3	R_4
8a	H	H	Ph	H
b	H	Ph	H	CH_3
c	CH_3	Ph	Ph	Ph
d	H	Ph	Ph	Ph

In 1972, the Isomura research group published a study of the thermal rearrangements in dilute solution of a series of 2-vinyl-2*H*-azirines.[7] The results of this study, which can again be explained by C–N cleavage leading to a vinyl nitrene, are displayed in Scheme III.

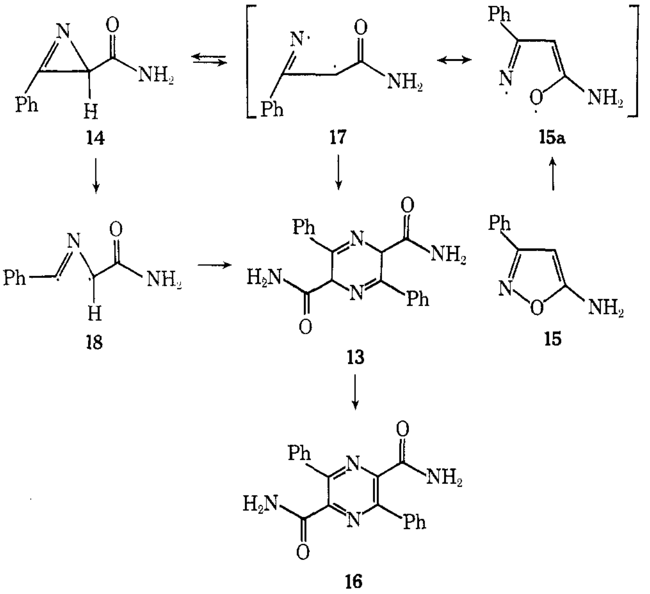
Rees and co-workers have subjected the series of 2*H*-azirines **9a–d** to flash-vacuum pyrolysis at 400–500 °C.[8] Their results may also be accounted for by initial carbon–nitrogen bond cleavage (Scheme IV). Nishiwaki and co-workers[9] have reported results describing the neat pyrolysis of 2*H*-azirine-2-carboxamides (**14**) and 5-aminoisoxazoles (**15**). The authors suggest that intermediate **17** has diradical character, but a vinyl nitrene would also be consistent with the reaction products. Nishiwaki points out that cleavage of the azirine C–C bond to form intermediate **18** is also a mechanistic possibility (Scheme V).

Scheme IV



9a, R_1 = Ptl; R_2 = Ph; R_3 = Me
b, R_1 = Ptl; R_2 = R_3 = Ph
c, R_1 = Ptl; R_2 = R_3 = Me
d, R_1 = Ptl; R_2 = Me; R_3 = Ph
(Ptl = phthalimido)

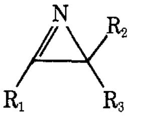
Scheme V



As a result of our interest in bond-breaking phenomena in small ring compounds,[10] we chose to study the thermal decompositions of substituted 2*H*-azirines. The original intent of this work was to elucidate the nature of the intermediate formed upon thermal C–N bond cleavage in 2*H*-azirines. However, the formation of unexpected products indicated that we had uncovered the first clear-cut example of products formed from carbon–carbon bond cleavage as a major pathway in 2*H*-azirine thermal decomposition, leading to formation of iminocarbenes.

Results

In the course of our work, it was necessary to synthesize azirines **19a–d.** Compounds **19a** and **19b** were prepared via the vinyl azide route of Hassner[11a,b] and **19c** and **19d** were synthesized from the appropriate dimethylhydrazone methiodide.[12a,b] These materials were subjected to pyrolysis in a quartz flow system at atmospheric pressure using helium as a carrier gas. Typical residence times in the pyrolysis zone were approximately 10 s. Products were condensed in a double U-tube trap at −196 °C.

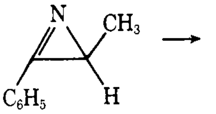


19a, R_1 = Ph; R_2 = Me; R_3 = H
b, R_1 = Ph; R_2 = Et; R_3 = H
c, R_1 = Ph; R_2 = R_3 = Me
d, R_1 = Me; R_2 = Ph; R_3 = Me

Polymerization of some of the pyrolysis products in the collection trap was a troublesome problem in this work. Extensive efforts were made to minimize polymerization; nevertheless 30–40% polymeric material was isolated from every pyrolysis. Even though the yield of polymer varied by as much as 10%, the proportions of apparently nonpolymerizing products remained constant in separate pyrolyses at a given temperature.

Pyrolysis (cf. Chart I) of 2-methyl-3-phenyl-2*H*-azirine (**19a**) at 565 °C consumed all the starting material. The monomeric products formed were styrene (56%) and benzonitrile (2%) (presumably HCN was also formed; vide infra). Fragmentation products of styrene comprised 4% of the pyrolysate and included ethylbenzene, toluene, and benzene. The pyrolysis of **19a** at several lower temperatures was monitored by vapor phase chromatography. No buildup of intermediate products was observed at 320 (0% conversion), 390, 466, or 523 °C.

Chart I. Products of the 565 °C Pyrolysis of 2-Methyl-3-phenyl-2*H*-azirine (19a)



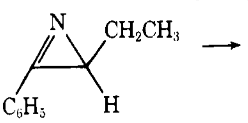
19a

$C_6H_5—CH=CH_2$ + $C_6H_5—C≡N$ + polymer + other

56% 2% 38% 4%

The apparent generality of this unexpected fragmentation for 2-alkyl-3-phenyl-2*H*-azirines was demonstrated by pyrolysis of **19b** at 565 °C (Chart II) ("other" includes mainly fragmentation products of β-methylstyrene, i.e., ethylbenzene, toluene, and benzene). *trans*- and *cis*-β-methylstyrene equilibrate thermally at 565 °C; the observed trans:cis ratio of 2:1 is the equilibrium mixture at this temperature.

Chart II. Products of the 565 °C Pyrolysis of 2-Ethyl-3-phenyl-2*H*-azirine (19b)



19b

$C_6H_5—CH=CH—CH_3$ + $C_6H_5—CH=CH_2$ + $C_6H_5—C≡N$

cis and trans 9% 2%

42%

polymer + other

39% 8%

In order to explain the formation of styrenes from **19a** and **19b**, bonding between C-3 of the azirine ring and the substituent carbon attached to C-2 must occur during the course of reaction. Two possible mechanistic routes which accomplish the observed transformation are shown in Scheme VI; however, neither path seems particularly reasonable as written. In path A, the azirine **20** (which has a hydrogen substituent at the 3 position) would be expected to rapidly decompose under our reaction conditions.[8,13] However, the first step in this mechanism involves an unprecedented 1,3-alkyl shift in an unsaturated ring. Path B involves carbon–carbon bond cleavage and 1,4-carbene insertion into a C–H bond to form azetine **22**.[14] Jones[15] has observed a case in which a carbene does presumably insert to form a four-membered ring; however, hydrogen abstraction would be expected to be a more facile process than C–H insertion in our system. In 1971 Hassner reported that cyclopropyl azides smoothly decompose to azetines and olefinic fragmentation products.[16] He suggested that the olefins could be coming from azetine decomposition, but does not rigorously prove it.

Scheme VI

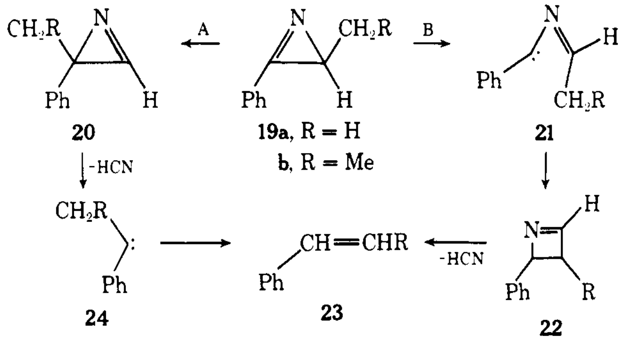
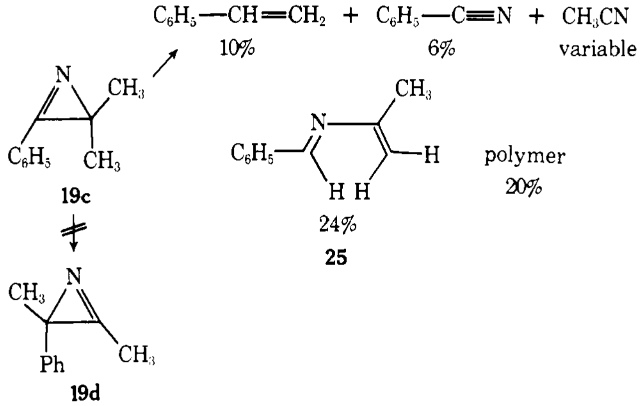


Chart III. Products of the 472 °C Pyrolysis of 2,2-Dimethyl-3-phenyl-2*H*-azirine (19c)



$C_6H_5—CH=CH_2$ + $C_6H_5—C≡N$ + CH_3CN

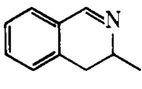
10% 6% variable

24% polymer 20%

Path A is relatively easy to test. Pyrolysis of **19c** should result in formation of **19d** (isolable at partial conversion temperatures) if 1,3-alkyl shifts are important in 2*H*-azirine decomposition. Also, acetonitrile should be the other fragmentation product, analogous to the presumed HCN obtained from decomposition of **19a**.

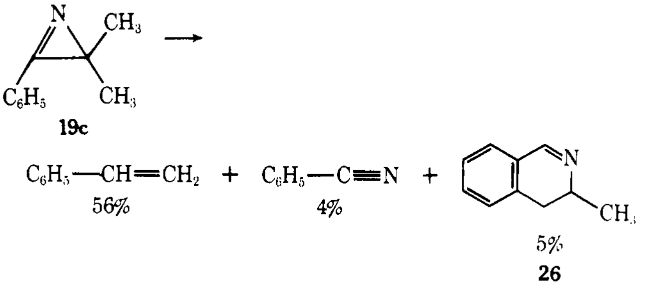
In analogy with **19a** and **19b**, pyrolysis of **19c** at 472 °C (60% conversion) also gave styrene and benzonitrile (Chart III). *No* methyl-shifted azirine **19d** was observed (nor was its thermal decomposition product; vide infra) but acetonitrile in variable amounts was detected in this case. In addition, a significant new product was obtained in 24% yield; its spectral data were consistent with azabutadiene **25**. In confirmation of this assignment, hydrolysis[17] of **25** in aqueous mineral acid gave benzaldehyde and acetone.

Formation of **25** provided the needed clue to understanding the mechanism of these pyrolyses, since we were able to show that it was converted to styrene under the reaction conditions. At higher temperatures (545 °C), **25** gave a 14:1 ratio of styrene and 3-methyldihydroisoquinoline (**26**). Pyrolysis of the 2*H*-azirine **19c** at 545 °C gave an ~11:1 ratio of styrene and **26** (Chart IV). The similar ratios of styrene and **26** in the azirine **19c** and azabutadiene (**25**) 545 °C pyrolyses strongly implicate **25** as the major primary pyrolysis product of **19c**.



26

Chart IV. Products of the 545 °C Pyrolysis of 2,3-Dimethyl-3-phenyl-2*H*-azirine (19c)



$C_6H_5—CH=CH_2$ + $C_6H_5—C≡N$ +

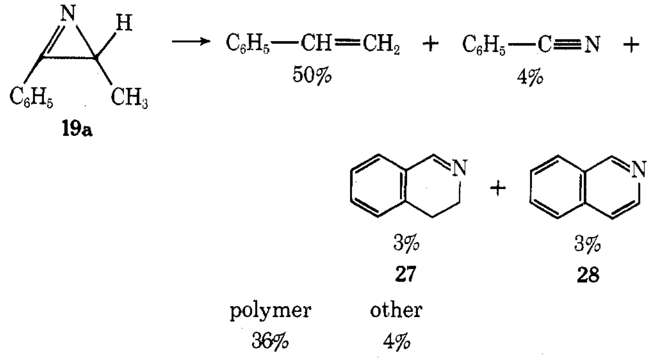
56% 4% 5%

polymer other

32% 3%

We were unable to isolate an azabutadiene intermediate from the pyrolysis of 2-methyl-3-phenyl-2*H*-azirine (**19a**). Apparently the azabutadiene is involved in the polymerization process, and its rate for polymerizing or fragmentation to styrene precludes its isolation. Nevertheless, the higher temperature conversion of azabutadiene (**25**) to the new product, dihydroisoquinoline (**26**), provided a possible test for the presence of an azabutadiene in the pyrolysis of **19a**. Since formation of **26** became competitive with fragmentation to styrene at higher temperatures, **19a** was pyrolyzed at 580 °C in anticipation of isolating 3,4-dihydroisoquinoline. Our hopes were realized, as demonstrated in Chart V.

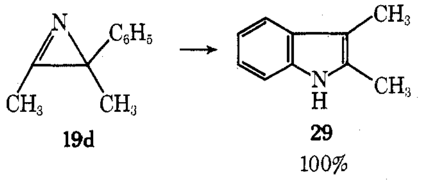
Chart V. Products of the 580 °C Pyrolysis of 2-Methyl-3-phenyl-2*H*-azirine (**19a**)



The oxidation of dihydroisoquinoline (**27**) to isoquinoline (**28**) at these temperatures is precedented by the high-temperature dihydronaphthalene to naphthalene conversion.[18] Isolation of the dihydroisoquinoline at higher temperatures strongly suggests that **19a** is also isomerizing to an azabutadiene.

The intervention of a competing alkyl-shift isomerization path (path A, Scheme VI) was rigorously ruled out by independent synthesis and pyrolysis of the "alkyl-shifted azirine" **19d** (Chart VI). Quantitative conversion of **19d** to the indole **29** is indicative of ring opening to the vinyl nitrene which then inserts into a phenyl C–H bond (Scheme II).

Chart VI. Products of the 480 °C Pyrolysis of 2,3-Dimethyl-2-phenyl-2*H*-azirine (**19d**)



The formation of acetonitrile from **19c** suggests that HCN is, in fact, the small molecule which is extruded during the pyrolysis of **19a** and **19b**. Our inability to isolate acetonitrile in an amount equivalent to styrene (from the **19c** pyrolyses) initially proved disconcerting, especially when control experiments established that acetonitrile could be recovered quantitatively after passing it through the pyrolysis system at 545 °C. However, when a ~5:1 *mixture* of azirine **19c** and acetonitrile was pyrolyzed at 470 °C, *no* acetonitrile was isolated. This more accurate control experiment suggests strongly that acetonitrile is in fact polymerizing under the reaction conditions. Also, the proportion of azabutadiene (**25**) was reduced from 24% (Chart III) to 7% in this pyrolysis; it appears that azabutadiene is also involved in the polymerization.

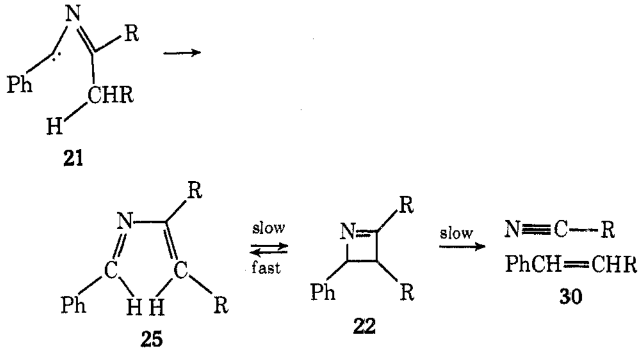
Efforts to retard the polymerization by copyrolysis of **19c** with solvent (and also by trapping the pyrolysate in solvent) were attempted with some success. A tenfold excess of diethyl ether was mixed with azirine **19c** in the vapor phase just outside the oven. The product traps contained an additional threefold excess of frozen diethyl ether prior to pyrolysis. In this manner, acetonitrile was isolated in 55% yield relative to styrene in one pyrolysis at 470 °C. However, these results were not reproducible; recovery of acetonitrile in 10% yield relative to styrene was a more typical result. Control experiments demonstrated the stability of diethyl ether to the reaction conditions.

Discussion

The results outlined above indicate that (1) carbon–carbon bond cleavage occurs upon thermolysis of 3-phenyl-2-alkyl-2*H*-azirines, (2) azabutadienes are primary pyrolysis products and precursors to the fragmentation products (styrenes and presumably nitriles), and (3) the azabutadiene to dihydroisoquinoline rearrangement is a competitive process at higher temperatures. Mechanistic questions which we will try to answer include (1) How do azabutadienes lead to the observed fragmentation products? (2) What is the nature of the species formed upon carbon–carbon bond rupture? (3) Why does this particular family of azirines (**19a–c**) display this behavior? (4) How does dihydroisoquinoline formation from azabutadienes occur?

The detection of azabutadienes as pyrolysis products makes reconsideration of path B in Scheme VI worthwhile. However, rather than postulating C–H insertion by the initially formed[22] carbene **21**, we believe that hydrogen abstraction occurs to form the imine **25** (1,4-hydrogen abstraction by vinyl carbene- or 1,3-diradical-like species, generated from thermal ring opening of substituted cyclopropenes, has ample precedent;[10,19–21] 1,3-butadienes comprise a significant portion of the pyrolysis products of alkyl-substituted cyclopropenes and have been postulated as being formed from vinyl carbene or 1,3-diradical species). An *endothermic* thermal electrocyclization may then generate a small steady state amount of azetine (**22**), which fragments to the observed products (Scheme VII);

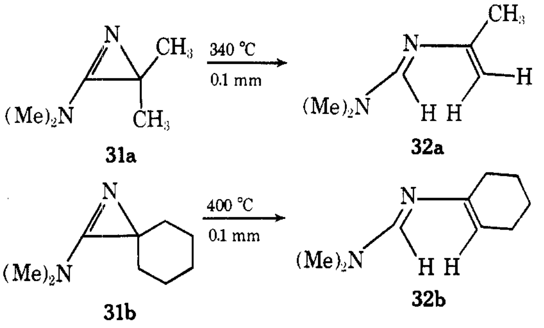
Scheme VII



Aue and Thomas have recently invoked a similar azetine–azabutadiene equilibrium to explain results in the gas-phase pyrolysis of 2-alkoxy-1-azetines.[23a] Additional support for 1,4-hydrogen transfer in iminocarbenes is provided by the very recent work of Ghosez and co-workers.[23b] These workers have shown that 3-amino-2-alkyl-2*H*-azirines **31a** and **31b** appear to be undergoing a similar C–C bond cleavage with subsequent formation of azabutadienes **32a** and **32b** (Scheme VIII). These authors report *no* fragmentation products analogous to the ones we observed, but this may be rationalized by considering that Ghosez' pyrolysis temperatures were 100–200 °C lower than in our work (where fragmentation was significant).[23b]

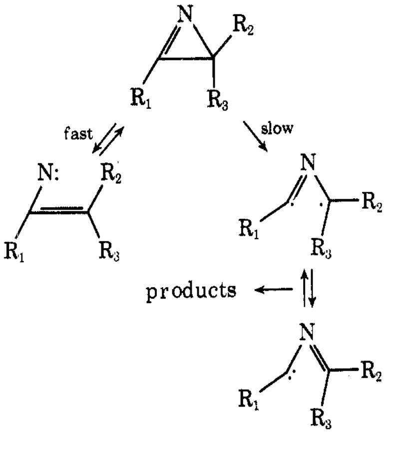
Our postulated azabutadiene–azetine equilibrium parallels the butadiene–cyclobutene thermal conversion. Brauman and Stephenson[24] have presented strong evidence that butadiene is in equilibrium with a small amount of cyclobutene at 637 °C in the gas phase.

Scheme VIII



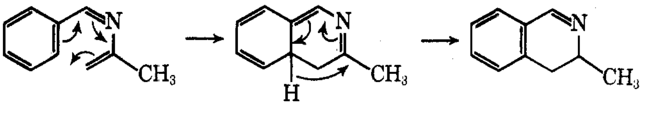
In our system the initial bond-breaking preference (C–N vs. C–C) has not been determined. N(sp^2)–C(sp^3) bonds are probably 5–10 kcal/mol weaker than C(sp^2)–C(sp^3) bonds. This guess is based solely on analogy to sp^3–sp^3 bond dissociation energies[25] in carbon and nitrogen systems; there are no values in the literature for the particular bond strengths in question. For all thermal azirine rearrangements investigated, other than ours and Ghosez',[23] *carbon–nitrogen* bond cleavage to form a vinyl nitrene seems to be the preferred bond-breaking process. It seems reasonable that C–N bond cleavage is also the lowest energy pathway in our system. However, by analogy with the work of Rees[8] (**9c** and **9d**, Scheme IV), the nitrene generated from **19a–c** will not undergo 1,4-hydrogen abstractions. The independent work of Isomura[6,7] and Rees[8] suggests that 1,2 abstraction by the nitrene (to form ketenimines) only occurs when hydrogen is the group being transferred. Consequently it is reasonable that no product-formation path, other than regeneration of the azirine, is available to the nitrene. Thus, reaction products are observed only when pyrolysis temperatures high enough to cause C–C cleavage are reached (Scheme IX). A test of this hypothesis awaits a more sophisticated experiment, such as the thermal racemization[10] of an optically active azirine.

Scheme IX



The conversion of azabutadiene (**25**) to dihydroisoquinoline (**26**) is a novel transformation in its own right. The first step of this process can be viewed as an electrocyclic ring closure of an azahexatriene to a 1,3-azacyclohexadiene. The second step simply involves a symmetry allowed, 1,5-suprafacial sigmatropic hydrogen migration (Scheme X). Weber and co-workers have recently observed the all-carbon analogue of this rearrangement; i.e., the conversion of phenyl-1,3-butadiene to dihydronapthalene.[26]

Scheme X



Experimental Section

A. Synthesis of Starting Azirines. 2-Ethyl-3-phenyl-2*H*-azirine (19b). Compound **19a** was prepared by photolysis of the corresponding azoalkene as described by Hassner,[11] and the same procedure was then applied to the synthesis of **19b**. After the solvent was removed by rotary evaporation, the azirine **19b** was vacuum transferred and purified by preparative VPC on column A (130 °C, 100 ml/min): ir 3090, 3060, 2980, 2960, 2900, 1746, 1615, 1508, 1480, 1470, 1395, 1340, 1321, 1165, 1088, 1045, 1003, 940, 910, 895, 705 cm^{-1}; NMR (CCl$_4$) δ 0.92 (t, 3 H, -CH$_2$CH$_3$), 1.35–1.90 (m, 2 H, -CH$_2$CH$_3$), 2.13 (t, 1 H, >CHCH$_2$), 7.38–8.00 (m, 5 H, phenyl).

2,3-Dimethyl-2-phenyl-2*H*-azirine (19d). Compound **19c** was prepared as described by Leonard,[12] and the method was then extended to the synthesis of **19d** (starting with 3-phenyl-2-butanone). This azirine was obtained in 30% yield and was purified by preparative VPC on column A (130 °C, 100 ml/min): ir 3050, 2980, 2960, 2890, 1775, 1615, 1510, 1460, 1445, 1392, 1380, 1279, 1082, 1045, 823, 710 cm^{-1}; NMR (CCl$_4$) δ 1.60 (s, 3 H, (Ph)C–CH$_3$), 2.34 [s, 3 H, -(CN)CH$_3$], 6.90–7.50 (m, 5 H, phenyl); high-resolution mass calcd, 145.089145; high-resolution mass observed, 145.0888.

B. Vapor Phase Chromatographic Analysis. All analytical vapor phase chromatography was performed on a Hewlett-Packard 5750 research chromatograph equipped with a Hewlett-Packard 3370A digital integrator. The chromatograph was equipped with a flame ionization detector. Preparative vapor phase chromatography was performed on a Varian Aerograph 90-P3 chromatograph equipped with a thermal conductivity detector. The following columns were used: column A, 10 ft × 0.375 in., 20% UCW-98, on 60/80 Chromosorb WAW-DMCS, glass; column B, 10 ft × 0.25 in., 10% DEGS on 60/80 Chromosorb P-NAW, glass; column C, 10 ft × 0.25 in., 30% SE-30 on 60/80 Chromosorb WAW-DMCS, glass; column D, 8 ft × 0.125 in., 10% SE-30 on 100/120 Chromosorb WAW-DMCS, aluminum; column E, 12 ft × 0.125 in., 15% DEGS on 100/120 Chromosorb WAW-DMCS, aluminum.

C. Pyrolyses. Flow pyrolyses were carried out utilizing a 1.2 cm o.d. quartz tube flow system contained in a Hoskin's tube furnace. Auxiliary heating wires, wrapped with asbestos tape, prevented sample condensation in the flow system at both the inlet and outlet sides. The pyrolysis products were collected in a double U-tube trap filled with Pyrex helices and maintained at −196 °C. Drying towers attached to the traps prevented condensation of moisture in the traps. The temperature of the quartz tube was monitored by an iron–constantan thermocouple. The neat reactants were introduced into the pyrolysis zone by a flow of helium (200 ml/min).

In a typical pyrolysis, 50–500 mg of VPC-purified starting material was carried through the reaction zone over the course of several hours. The pyrolysate was immediately taken up in diethyl ether to minimize polymerization in the collection traps.

Initial pyrolyses were carried out at a temperature where a given azirine was just quantitatively consumed. At these temperatures (typically 500–600 °C) monomeric product accounted for 55–65% of the pyrolysate. A reddish polymeric material comprised the remainder of the pyrolysate. Mass balance experiments confirmed that all starting material is accounted for by the trapped monomers and polymer. Relative flame ionization detector sensitivities were determined for all pyrolysis products by analysis of a solution containing known amounts of the products.

The possibility of materials reacting on the surface of the flow system was ruled out by performing a packed-tube pyrolysis. The quartz tube was packed with 1 × 0.2 cm o.d. pieces of quartz tubing. Comparison of open- and packed-tube pyrolyses showed no surface-enhanced reactions to be occurring.

1-Phenyl-3-methyl-2-aza-1,3-butadiene (25). 25 was isolated from a concentrated diethyl ether solution of the 472 °C flow pyrolysis products of **19c** by preparative VPC on column B (100°, 80 ml/min): ir 3040, 3005, 2950, 2900, 2850, 1642, 1616, 1571, 1488, 1447, 1360, 1304, 1257, 1205, 1165, 967, 950, 870, 845, 711, 682 cm^{-1}; NMR (CCl$_4$) δ 2.00 (s, 3 H, vinyl -CH$_3$), 4.48 (s, 1 H, vinyl H), 4.69 (s, 1 H, vinyl H), 7.30–8.90 (m, 5 H, phenyl), 8.18 (s, 1 H, imino H). Anal. Calcd for C$_{10}$H$_{11}$N: C, 82.76; H, 7.59; N, 9.66. Found: C, 82.42; H, 7.74; N, 9.84.

The structure of **25** was proved by hydrolysis[17] of a solution of 0.010 g of **25** in 0.100 g of 2-butanone with 1.250 ml of a 10% aqueous HCl solution. The reaction mixture was stirred for 48 h at room temperature. Work-up involved neutralizing with aqueous Na$_2$CO$_3$ and extraction into ether. Rigorous spiking experiments on two analytical VPC columns [columns D and E (various temperatures, 80–115 °C, 30 ml/min)] showed the hydrolysis products to have VPC retention times identical with those of authentic samples of benzaldehyde and acetone. The later eluting product was isolated from the hydrolysis extracts by preparative VPC on column B (70 °C and 70 ml/min). This compound's ir spectrum correlated exactly with that of an authentic sample of benzaldehyde.

2,3-Dimethylindole (29). The indole was isolated by preparative VPC from an ether solution of the 480 °C pyrolysate of **19d**. The ir spectrum correlated exactly with ir spectrum 911G, Aldrich Library, for 2,3-dimethylindole: ir 3492, 3060, 2940, 2880, 1625, 1550, 1476, 1346, 1310, 1270, 1253, 1010, 932, 730 cm^{-1}; NMR (CCl_4) δ 2.19 (s, 3 H, 3-CH_3), 2.32 (s, 3 H, 2-CH_3), 6.50–6.85 (broad, 1 H, NH), 6.90–7.45 (m, 4 H, phenyl).

3,4-Dihydroisoquinoline (27). This compound was isolated by preparative VPC of the 580 °C pyrolysate of **19a** on column C (100 °C, 100 ml/min); ir 3100, 3040, 2970, 2920, 2878, 1626, 1576, 1484, 1452, 1443, 1426, 1294, 1272, 1204, 1188, 1113, 1051, 1029, 1000, 951, 918, 873, 857, 683 cm^{-1}; NMR (CCl_4) δ 2.67 (t, J = 7.1 Hz, 2 H, NCH_2CH_2), 3.73 (t of d, J = 7.1, 2.1 Hz, 2 H, NCH_2CH_2), 6.95–7.42 (m, 4, aromatic), 8.17 (t, J = 2.1 Hz, 1 H, imino H). The structure proof was confirmed by oxidation at 530 °C over Pd/C in a quartz flow system. Oxidized product spectra correlated exactly with those of authentic isoquinoline.

Isoquinoline (28). The 580 °C pyrolysis of **19a** produces isoquinoline, presumably from oxidation of 3,4-dihydroisoquinoline.[18] This pyrolysis product was isolated by preparative VPC of a concentrated ether solution of the pyrolysate (column C, 100 °C, 100 ml/min): ir 3080, 3002, 2987, 1628, 1589, 1574, 1505, 1382, 1375, 1270, 1247, 1213, 1136, 1033, 1011, 941, 853, 816 cm^{-1}; NMR (CCl_4) δ 6.90–8.2 (m, 6 H), 5.58 (d, 1 H), 6.29 (s, 1 H). The spectral data correlated exactly with the spectra of an authentic sample of isoquinoline.

3,4-Dihydro-3-methylisoquinoline (26). 26 was isolated from a concentrated ether solution of **19c** by preparative VPC on column C (100 °C, 100 ml/min): ir 3078, 3040, 2980, 2943, 2897, 2840, 1670, 1585, 1500, 1468, 1439, 1390, 1368, 1327, 1304, 1227, 1211, 1141, 1130, 1058, 1043, 960, 943, 930, 898, 820, 709 cm^{-1}; NMR (CCl_4) δ 1.31 (d, J = 6.8 Hz, 3 H, $-CH_3$), 2.68 (d, J = 4.0 Hz, 2 H, CH_3CHCH_2-), 3.32–4.90 (m, 1 H, $-CHCH_3$), 6.90–7.40 (m, 4 H, aromatic), 8.18 (d, J = 2.2 Hz, 1 H, imino H); mass spectrum M^+ m/e 145, 144, 130, 117, 103, 90, 76, 77, 51, 27. This dihydroisoquinoline was oxidized in the same manner as described for 3,4-dihydroisoquinoline (27). In the course of oxidation, the methyl group was cleaved, and isoquinoline was obtained.

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Registry No.—**19a,** 16205-14-4; **19b,** 51209-52-0; **19c,** 14491-02-2; **19d,** 57573-53-2; **25,** 51209-53-1; **26,** 14123-78-5; **27,** 3230-65-7; **28,** 119-65-3; **29,** 91-55-4.

References and Notes

(1) A preliminary account of this work has been published. L. A. Wendling and R. G. Bergman, *J. Am. Chem. Soc.*, **96**, 308 (1974).

(2) Camille and Henry Dreyfus Foundation Teacher-Scholar Grant Awardee, 1970–1975.

(3) (a) A. Padwa and S. I. Wetmore, Jr., *J. Am. Chem. Soc.*, **96**, 2414 (1974); (b) A. Padwa and J. Smolanoff, *ibid.*, **93**, 549 (1971); (c) A. Padwa and J. Smolanoff, *J. Chem. Soc., Chem. Commun.*, 342 (1973); (d) A. Padwa, J. Smolanoff, and A. Tremper, *J. Am. Chem. Soc.*, **97**, 4682 (1975).

(4) (a) H. Giezendanner, M. Marky, B. J. Jackson, H.-J. Hansen, and H. Schmid, *Helv. Chim. Acta*, **55**, 545 (1972); (b) B. Jackson, H.-J. Hansen, and H. Schmid, *ibid.*, 119 (1972); (c) N. Gakis, M. Marky, and H. Schmid, *ibid.*, 748 (1972); (d) B. Jackson, N. Gakis, M. Marky, H.-J. Hansen, W. von Philipsborn, and H. Schmid, *ibid.*, 916 (1972); (e) W. Sieber, P. Gilgen, S. Chaloupka, H.-J. Hansen, and H. Schmid, *Helv. Chim. Acta*, **56**, 1679 (1973).

(5) L. Salem, *J. Am. Chem. Soc.*, **96**, 3486 (1974).

(6) K. Isomura, S. Kobayashi, and H. Taniguchi, *Tetrahedron Lett.*, 3499 (1968).

(7) K. Isomura, M. Okada, and T. Taniguchi, *Chem. Lett.*, 629 (1972).

(8) D. J. Anderson, T. L. Gilchrist, G. E. Gymer, and C. W. Rees, *Chem. Commun.*, 1518 (1971).

(9) (a) T. Nishiwaki, *Tetrahedron Lett.*, 2049 (1969); (b) T. Nishiwaki, A. Nakano and H. Matsuoka, *J. Chem. Soc. C*, 1825 (1970).

(10) E. J. York, W. Dittmar, J. R. Stevenson, and R. G. Bergman, *J. Am. Chem. Soc.*, **95**, 5680 (1973).

(11) (a) A. Hassner and F. W. Fowler, *J. Am. Chem. Soc.*, **90**, 2869 (1968); (b) F. W. Fowler, Ph.D. Thesis, University of Colorado, Boulder, Colo., 1968.

(12) (a) N. J. Leonard and B. Zwanenburg, *J. Am. Chem. Soc.*, **89**, 4456 (1967); (b) R. F. Parcell, *Chem. Ind.* (*London*), 1396 (1963).

(13) K. Isomura, M. Okada, and H. Taniguchi, *Tetrahedron Lett.*, 4073 (1969).

(14) We do not know of any precedent for a nitrene C–H insertion to form a four-membered ring.

(15) D. C. Richardson, M. E. Hendrick, and M. Jones, Jr., *J. Am. Chem. Soc.*, **93**, 3790 (1971).

(16) A. B. Levy and A. Hassner, *J. Am. Chem. Soc.*, **93**, 2051 (1971).

(17) A. Hassner, J. O. Currie, Jr., A. S. Steinfeld, and R. F. Atkinson, *J. Am. Chem. Soc.*, **95**, 2982 (1973).

(18) (a) G. M. Badger and T. M. Spotswood, *J. Chem. Soc.*, 1635 (1959); (b) T. M. Spotswood, *ibid.*, 4427 (1960).

(19) (a) R. Srinivasan, *J. Am. Chem. Soc.*, **91**, 6250 (1969); (b) R. Srinivasan, *J. Chem. Soc. D*, 1041 (1971).

(20) M. A. Battiste, B. Halton, and R. H. Grubbs, *Chem. Commun.*, 907 (1967).

(21) R. D. Streeper and P. D. Gardner, *Tetrahedron Lett.*, 767 (1973).

(22) (a) Because of the extremely high energies required to generate zwitterions in the gas phase,[22b] we prefer to write species such as **26** as neutral carbene or diradical, rather than dipolar, intermediates; (b) L. Salem and C. Rowland, *Angew. Chem.*, **11**, 92 (1972).

(23) (a) D. H. Aue and D. Thomas, *J. Org. Chem.*, **40**, 1349 (1975); (b) A. Demoulin, H. Gorissen, A.-M. Hesbian-Frisque, and L. Ghosez, *J. Am. Chem. Soc.*, **97**, 4409 (1975).

(24) L. M. Stephenson, R. V. Gemmer, and J. I. Brauman, *J. Am. Chem. Soc.*, **94**, 8620 (1972).

(25) S. W. Benson, "Thermochemical Kinetics", Wiley, New York, N.Y., 1968, p 215.

(26) P. B. Valkovich, J. L. Conger, F. A. Castiello, T. D. Brodie, and W. P. Weber, *J. Am. Chem. Soc.*, **97**, 90 (1975).

A Convenient Two-Step Synthesis of 4-(2-Imidazolyl)phthalazones from *o*-Phthaloyl Dichloride

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The imidazo[1,2-*b*]isoquinoline-5,10-diones (**3**) derived from the condensation of equimolar amounts of *o*-phthaloyl dichloride (**1**) and an imidazole (**2**) in the presence of 2 molar equiv of Et_3N, react readily with hydrazines R_3NHNH_2 (R_3 = H, alkyl, aryl) to form 4-(2-imidazolyl)phthalazones (**4**), a new class of compounds. The reactions of these carbonyl reagents differ from those of nucleophiles such as hydroxide ion, alcohols, and amines which attack **3** at the lactam carbonyl group and form the carboxylic acid derivatives (**5–7**).

The patent literature[1,2] describes the condensation of equimolar amounts of *o*-phthaloyl dichloride (**1**) and imidazoles or benzimidazoles (**2**) possessing unsubstituted 1 and 2 positions in CH_3CN containing 2 molar equiv of Et_3N to produce imidazo[1,2-*b*]isoquinoline-5,10-diones (**3**), which react with nucleophiles such as hydroxide ion,