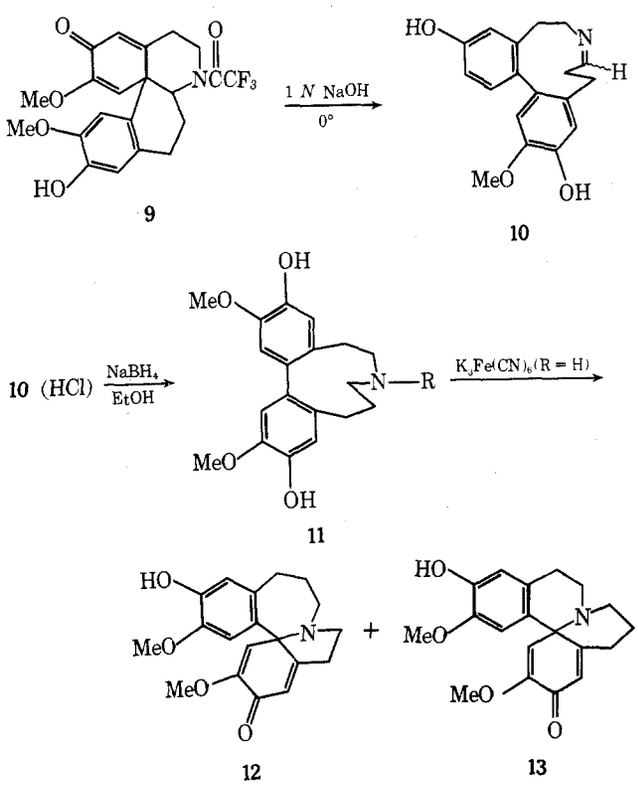
Scheme II



CH_3CO). It was our original intention to affect the oxidation of the trifluoroacetamide of **11** in order to produce the corresponding diphenoquinone. A suitably substituted dipheno-*p*-quinone could then be transformed into the cephalotaxine precursor **7** via an intramolecular Michael addition of the nitrogen.[5] Attempted oxidation of **11** (R = CH_3CO) with dichlorodicyanoquinone, potassium hexacyanoferrate, silver oxide, or the ferric chloride–DMF complex[12] yielded only starting material. Thallium trifluoroacetate oxidation of the trifluoroacetamide of **11** (R = CH_3CO) produced a dimer (35% yield) derived from oxygen–carbon coupling. Lead tetraacetate oxidation of **11** (R = CH_3CO) in glacial acetic acid produced in high yield a bis-*o*-quinol acetate. The above results reflect the difficulty in oxidizing **11** (R = CH_3CO) to the corresponding dipheno-*p*-quinone, presumably because of the orthogonality of the aromatic rings of **11**. Thus, each aromatic ring of **11** (R = CH_3CO) behaves independently toward oxidation.

In contrast to the oxidations of the trifluoroacetamide of **11**, the free amine **11** (R = H) was cleanly transformed into two cyclized homoerythrina skeletons with potassium hexacyanoferrate in methylene chloride–sodium bicarbonate solution. After preparative layer chromatography on silica gel of the crude reaction mixture, a 45% yield of crystalline dienone **12** (mp 166–167°, from 2-propanol) was isolated along with 15% crystalline homoerysodienone **13** (mp 195.5–197.5°, from 2-propanol) and 35% recovered starting bisphenolic amine **11** (R = H). The isolation of the schelhammera-type skeleton[13] **12** and the new homoerysodienone skeleton **13** is consistent with standard phenolic coupling of the amine nitrogen para to a free hydroxyl group (paths a and b, Scheme I). The ratio of **12** to **13** is probably a good indication of the conformational preference for ring closure via path a vs. closure via path b. That no cephalotaxine precursor (path c) was observed in the above oxidation suggests the absence of a dipheno-*p*-quinone intermediate or a suitably disposed *p*-hydroxy group (**5**, R_4 = H). We are presently exploring the preparation of the biscatechol derivative of **11** and its transformation into a cephalotaxine precursor, via an *o*-quinone.

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Department of Chemistry
The University of Michigan
Ann Arbor, Michigan 48104

Joseph P. Marino*
James M. Samanen

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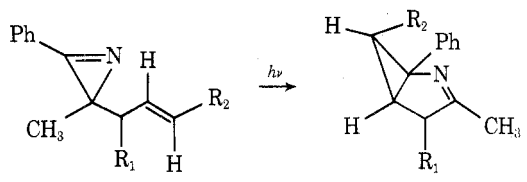
Thermal Rearrangement of Allyl Substituted 2*H*-Azirines to 3-Azabicyclo[3.1.0]hex-2-enes

Summary: The thermal rearrangement of 2-allyl substituted 2*H*-azirines to 3-azabicyclo[3.1.0]hex-2-enes proceeds in high yield. The reactions can best be rationalized in terms of an equilibration of the 2*H*-azirine with a transient vinyl nitrene which subsequently adds to the adjacent π bond.

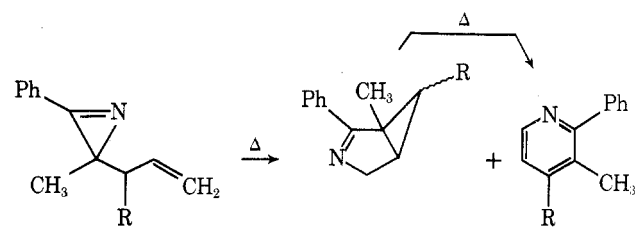
Sir: Photolysis of 2*H*-azirines leads to irreversible ring opening and the formation of nitrile ylides as intermediates.[1,2] These species may be intercepted by a variety of dipolarophiles to form five-membered heterocyclic rings. In certain cases the initially formed 1,3 dipole can be intramolecularly trapped[3] to give novel azabicyclohexenes.[4] For example, irradiation of allyl substituted 2*H*-azirines (**1**) produce 2-azabicyclo[3.1.0]hex-2-enes (**2**) via an unusual 1,1 cycloaddition reaction of the 1,3 dipole.[4] This observation stimulated us to begin a general investigation of the scope and mechanistic details of the intramolecular cyclization of unsaturated azirines. In this communication we wish to report on the thermolysis of a number of allyl substituted

2*H*-azirines and the formation of products previously unobserved in both thermal[5] and photochemical[1,2] azirine decompositions.



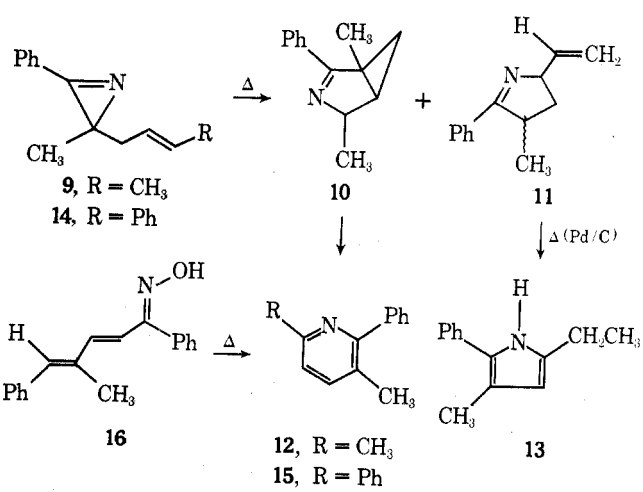
1 2

Thermolysis of 2-phenyl-3-methyl-3-allylazirine[6] (**3**) in toluene at 195° for 180 hr or in the absence of solvent at 250° for 1.5 hr gave 1-methyl-2-phenyl-3-azabicyclo-[3.1.0]hex-2-ene (**4**, 90%) and 3-methyl-2-phenylpyridine (**5**, 10%). The identity of **4** was determined by its straightforward spectral characteristics[7] as well as its facile conversion into **5** (picrate mp 164–165°)[8] on further heating. Thermolysis of the closely related methyl substituted azirine **6** gave 1,6-dimethyl-2-phenyl-3-azabicyclo[3.1.0]hex-2-ene (**7**, 58%) as a 1:1 mixture of endo and exo isomers[9] as well as 3,4-dimethyl-2-phenylpyridine (**8**, 25%) (picrate mp 171–172°).[10] The mixture of exo and endo isomers of **7** were smoothly converted into pyridine **8** on further heating.



3, R = H; **6**, R = CH_3 **4**, R = H; **7**, R = CH_3 **5**, R = H; **8**, R = CH_3

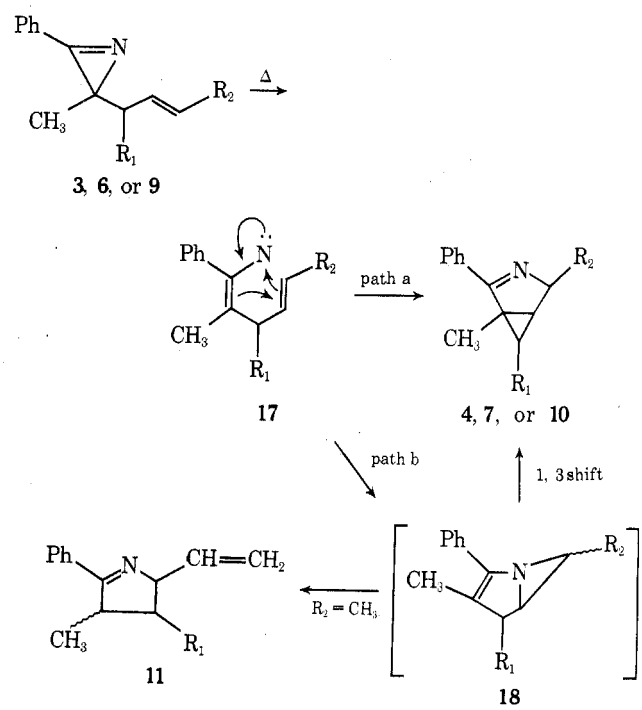
Subjection of azirine **9** to similar pyrolysis conditions gave 1,4-dimethyl-2-phenyl-3-azabicyclo[3.1.0]hex-2-ene[11] (**10**, 71%), 2-phenyl-3-methyl-5-vinyl-Δ^1-pyrroline[12] (**11**, 23%), as well as a trace amount (<5%) of 3,6-dimethyl-2-phenylpyridine (**12**).[10] The structure of Δ^1-pyrroline **11** was confirmed by refluxing **11** in toluene in the presence of palladium on carbon (5%) for 48 hr. This resulted in the quantitative formation of 2-phenyl-3-methyl-4-ethylpyrrole (**13**). That Δ^1-pyrroline **11** did not arise from 3-azabicyclohexene **10** was shown by heating **10** under conditions similar to those used for the pyrolysis of azirine **9**. Under these conditions **10** was converted exclusively into pyridine **12**. The thermal rearrangement of 2-phenyl-3-methyl-3-cinnamylazirine (**14**) was also studied. Thermolysis of **14** gave 2,6-diphenyl-3-methylpyridine (**15**, 49%) as the only characterizable material. The structure of **15** was verified by comparison with an authentic sample prepared from the thermolysis of oxime **16**. In this case, there were no detectable quantities of a 3-aza substituted bicyclohexene. It would appear as though the initially formed azabicyclohexene is converted into pyridine **15** at a faster specific rate than it is formed.



9, R = CH_3; **14**, R = Ph **10** **11**

16 **12**, R = CH_3; **15**, R = Ph **13**

The thermal transformations observed with these systems can best be rationalized in terms of an equilibration of the 2*H*-azirine with a transient vinyl nitrene (**17**) which subsequently rearranges to the final azabicyclohexenes. The products formed on thermal decomposition of 2*H*-azirines generally appear to involve C–N rather than C–C bond cleavage.[13] In some cases, C–N bond cleavage ultimately leads to fragmentation of the three-membered ring with the subsequent formation of a nitrile and carbene[14] and in other cases results in the formation of indoles[15] or pyrroles.[16] One possible route by which the vinyl nitrene can rearrange to the final product (path a) involves attack of the neighboring π system on the electrophilic singlet nitrene followed by bond reorganization. An equally plausible mechanism (path b) involves intramolecular addition of



3, **6**, or **9** **17** **4**, **7**, or **10** **11** **18**

the nitrene onto the adjacent π bond to give a bicycloaziridine (**18**) as a transient intermediate.[17] This species can subsequently rearrange to the observed product by a 1,3-sigmatropic shift. The allowed concerted thermal 1,3 shift requires an inversion of the migration center, and this seems sterically prohibited in this system. Although a "forbidden" 1,3-suprafacial concerted process cannot be excluded,[18] the rearrangement of **18** to the observed azabicyclohexene probably involves a diradical intermediate by analogy to the results obtained with the parent carbocycle.[19,20] Some evidence favoring path b is provided by the isolation of Δ^1-pyrroline **11** from the thermolysis of **9**. The formation of this product can be rationalized as proceeding via a homo[1,5] hydrogen migration from the endo isomer of bicycloaziridine **18**.[21]

We are continuing to explore the scope and mechanistic details of this novel thermal reaction.

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(7) Compound **4**: uv (cyclohexane) 239 nm (ϵ 11 000); NMR δ 0.45 (t, 1 H, J = 4.0 Hz), 0.96 (dd, 1 H, J = 8.0 and 4.0 Hz), 1 43 (s, 3 H), 1.64 (m, 1 H), 3.75 (dd, 1 H, J = 17.5 and 2.0 Hz), 3.98 (dd, 1 H, J = 17.5 and 5.0 Hz), 7.2–7.8 (m, 5 H); *m/e* 171 (M^+).
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(9) Compound **7**: NMR (endo) δ 0.75 (d, 3 H, J = 6.0 Hz), 1.22 (d, q, 1 H, J = 8.0 and 6.0 Hz), 1.42 (s, 3 H), 1.62 (dd, 1 H, J = 8.0 and 2.0 Hz), 3.56 (dd, 1 H, J = 18.0 and 2.0 Hz), 3.93 (dd, 1 H, J = 18.0 and 7.0 Hz); NMR exo δ 0.70 (p, 1 H, J = 6.0 Hz), 1.19 (d, 3 H, J = 6.0 Hz), 1.25 (dd, 1 H, J = 5.0 and 2.0 Hz), 1.38 (s, 3 H), 3.78 (dd, 1 H, J = 17.0 and 2.0 Hz), 3.94 (dd, 1 H, J = 17.0 and 5.0 Hz).
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(11) Compound **10**: NMR δ 0.48 (t, 1 H, J = 4.0 Hz), 0.96 (dd, 1 H, J = 8.0 and 4.0 Hz), 1.25 (d, 3 H, J = 7.0 Hz), 1.46 (dd, 1 H, J = 8.0 and 4.0 Hz), 1.96 (s, 3 H), 3.87 (q, 1 H, J = 7.0 Hz), 7.2–7.9 (m, 5 H).
(12) Compound **11**: NMR δ 1.16 (two doublets, 3 H, J = 7.0 Hz), 1.90 (m, 1 H), 1.3–1.6 (m, 1 H), 3.36 (m, 1 H), 4.60 (m, 1 H), 4.9–5.3 (m, 2 H), 5.8–6.2 (m, 1 H), 7.0–7.9 (m, 5 H).
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Department of Chemistry
State University of New York
at Buffalo
Buffalo, New York 14214

Albert Padwa*
Per H. J. Carlsen

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