Phase-Dependent Stereochemistry and Chemical Activation in the Thermal Decomposition of 2,3-Diazabicyclo[2.1.1]hexene

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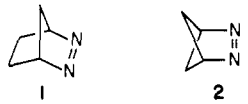
The thermal decomposition of five-membered cyclic 1,2-diazenes (1-pyrazolines) has been intensively investigated, although no fully satisfactory mechanistic scheme has been developed. The most intriguing aspect of these nitrogen extrusions is the stereochemistry, as both single and double inversions at the reacting carbon centers have been observed.[1] In the prototypical bicyclic pyrazoline, 2,3-diazabicyclo[2.2.1]heptene (**1**), the predominant pathway for



1

2

4

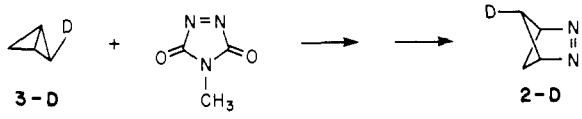
5

6

7

gas-phase decomposition is double inversion.[2] We have now determined the stereochemistry of nitrogen loss from the highly strained 2,3-diazabicyclo[2.1.1]hexene (**2**), only the second simple bicyclic diazene ring system to be so studied. We find complete scrambling on thermolysis in solution but a slight preference for double inversion in the gas phase. We have also found that the product distribution from gas-phase thermolysis of **2** is strongly pressure dependent, thus providing the first example of chemical activation in the thermal decomposition of a *symmetrical* 1,2-diazene.

Addition of *N*-methyltriazolinedione to *exo*-[2-^{2}H]-bicyclo-[1.1.0]butane (**3-D**),[3] under the conditions previously described,[5]



3-D 2-D

is completely stereospecific within the detection limits of 77.775-MHz ^{2}H NMR spectrometry. The ultimate product is **2-D**, with the deuterium exo to the molecule. The addition presumably involves a stepwise endo attack of the triazolinedione, as in related additions across strained C–C bonds.[6] Previous speculations concerning a possible exo attack in substituted derivatives of **3** are thus not relevant to the parent system.[7]

Thermolysis of **2-D** in benzene at 115 °C affords exclusively bicyclobutane (**3**),[5] with the label equally distributed between the exo and endo positions.[8] The simplest explanation of this result is that 1,3-cyclobutanediyl (**4**) is an intermediate in the reaction

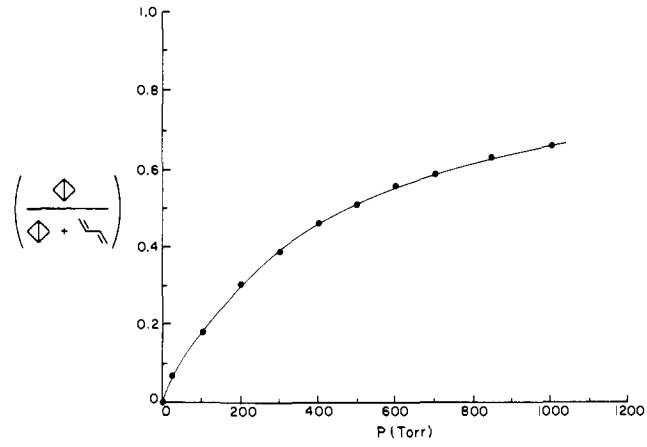


Figure 1. Product composition as a function of pressure for the gas-phase thermal decomposition of **2**.

sequence. Thus, the unusual stereochemical aspects of the decomposition of **1** and a variety of monocyclic pyrazolines[1] are absent in **2**.

Gas-phase pyrolysis of **2** is surprising in two respects. First, the bicyclobutane formed is not completely stereochemically randomized. The results suggest that 90% of the decomposition involves a stereorandom intermediate but the remaining 10% goes by a double-inversion pathway. Preliminary studies indicate that this result is independent of pressure, and it is at present unexplained.

Also in contrast to the solution chemistry, gas-phase thermolysis of **2** produces significant quantities of butadiene.[9] As shown in Figure 1, the product distribution is very strongly dependent on pressure, reaching 100% butadiene at low pressures (0.2 torr). It is known that bicyclobutane rearranges to butadiene (E_a = 40.6 kcal/mol),[10] and thus chemical activation is indicated. Only one other example of "hot molecule" chemistry from the thermal decomposition of a pyrazoline has been observed. Bergman found that pyrolysis of **5** at 1 atm gave 98% spiropentane, but at 0.2 torr this value drops to 81%, with the remainder being "hot molecule" products.[11] Interestingly, the isomeric, symmetrical pyrazoline **6** did not produce a "hot molecule" effect.[11] These results were interpreted by using a model proposed earlier by Bauer.[12] In the symmetrical diazene a symmetrical transition state was assumed, and thus the N_2 is formed with a stretched N–N bond. Since the N–N vibration is essentially perpendicular to the reaction path, coupling with the hydrocarbon fragment is poor, and the excess vibrational energy is carried off by N_2. In the unsymmetrical diazene, **5**, a single C–N cleavage produces an intermediate diazenyl biradical. This allows efficient vibrational mixing, and thus "hot" hydrocarbons can be formed.[12]

Since **2** shows a much wider product variation with pressure than **5** and since it is a symmetrical pyrazoline, we felt it was necessary to rule out alternative sources of butadiene. A well-precedented 1,2-H shift in biradical **4** would produce cyclobutene, which could then open to butadiene. Alternatively, allyldiazomethane (**7**) could be produced either by a retro[3 + 2]cycloaddition of **2** or by sequential C–N cleavage to a diazenyl biradical followed by C–C cleavage.[13] Loss of N_2 from **7** would produce a carbene which would give butadiene. Pyrolysis of **2-D**, however, allows a differentiation among the three mechanisms. Hydrogen shifts in biradical **4** would produce both [1-^{2}H]- and [3-^{2}H]-cyclobutene, in a ratio between 1:2 and 1:3, depending on the

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(2) Roth, W. R.; Martin, M. *Justus Liebigs Ann. Chem.* **1967**, *702*, 1–7. Allred, E. L.; Smith, R. L., *J. Am. Chem. Soc.* **1969**, *91*, 6766–75.
(3) **3-D** was prepared by the procedure of Wiberg[4] and contained 75% exo, 16% endo, and 9% bridgehead deuterium by 77.775-MHz ^{2}H NMR spectrometry. We refer to this species as *exo* labeled, and all subsequent experiments were analyzed based on this labeling pattern. Similar *exo/endo* stereoselectivity was observed by Wiberg,[4] but no bridgehead deuterium was seen, presumably because ^{1}H NMR spectrometry was used for analysis. The origin of the bridgehead deuterium is not known.
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(7) Amey, R. L.; Smart, B. E. *J. Org. Chem.* **1981**, *46*, 4090–2.
(8) It has previously been demonstrated[4] that *exo/endo* interconversion of **3-D** does not occur.
(9) Thermolyses were conducted in a static, 2-L Pyrex vessel at 120 °C. The bath gas was N_2. Products were analyzed by gas chromatography. Control experiments revealed that bicyclobutane was stable to the reaction conditions and that a significant change in the surface to volume ratio did not affect the product ratio.
(10) Frey, H. M.; Stevens, I. D. R. *Trans. Faraday Soc.* **1965**, *61*, 90.
(11) Shen, K. K.; Bergman, R. G. *J. Am. Chem. Soc.* **1977**, *99*, 1655–7.
(12) Bauer, S. H. *J. Am. Chem. Soc.* **1969**, *91*, 3688–9.
(13) Allyldiazomethane is formed upon photolysis of **2**. Chang, M. H.; Dougherty, D. A., submitted for publication.

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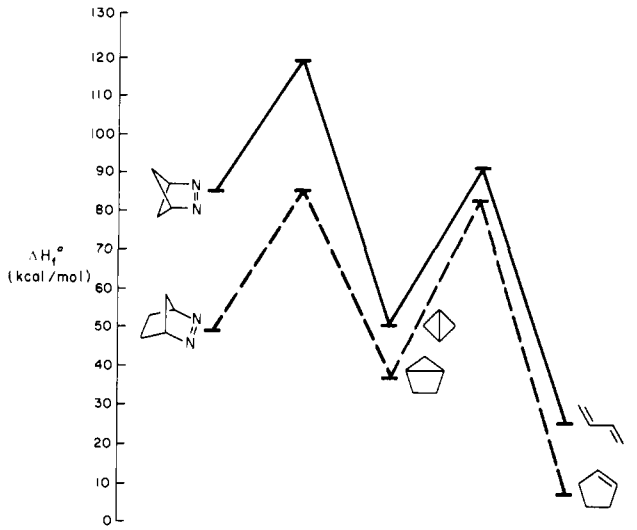

Figure 2. Energetics of the thermal decompositions of **1** and **2**.

magnitude of the kinetic isotope effect (KIE). These would then produce [2-^{2}H]- and [1-^{2}H]-butadiene, respectively. Diazoalkene **7** would be labeled equally in the allylic and vinylic CH_2 groups (ignoring the secondary KIE), and thus this route would produce a 1:1 mixture of [1-^{2}H]- and [2-^{2}H]-butadiene. However, it has been shown that [2-^{2}H]-bicyclobutane (**3-D**) produces only [1-^{2}H]-butadiene on thermolysis.[4] We find that gas-phase pyrolysis of **2-D** also produces only [1-^{2}H]-butadiene, consistent only with the "hot molecule" mechanism.

The reason that symmetrical diazene **2** shows such a large "hot molecule" effect can be seen in Figure 2, which compares the energetics of decomposition of **2** and **1**, the latter being considered a "typical" pyrazoline. Accurate activation parameters are available for all processes.[14] The heat of formation is known for each compound[15] except **2**, for which the value determined by molecular mechanics is used.[16] An error as large as 5 kcal/mol in this value would not affect the current analysis. In both cases a hydrocarbon is produced that could rearrange to another product if sufficient energy were available. The difference between **1** and **2** is that the transition state for the decomposition of **2** lies well above that for the hydrocarbon rearrangment. This is entirely a consequence of the high strain energy of **2**, which substantially raises ΔH_f° of **2** and its decomposition transition state. Even if a significant amount of excess energy is carried off by the N_2, there still could be enough energy to overcome the bicyclobutane rearrangement barrier. Thus, our results do not necessarily contradict the Bauer/Bergman analysis,[11,12] since the excess energy from **5** and **6** is much less than that from **2**. However, our results do require that a very substantial amount of the excess energy in the decomposition of **2** be localized in the hydrocarbon fragment, perhaps in the form of biradical **4**. This could indicate that the vibrational coupling in the symmetrical transition state is more effective than previously postulated[12] or the transition state for the decomposition of **2** is unsymmetrical.

Acknowledgment. We gratefully acknowledge the donors of the Petroleum Research Fund, administered by the American Chemical Society, the Research Corporation, the Camille and Henry Dreyfus Foundation, and the National Science Foundation (Grant CHE-8024664) for support of this work, and the use of the Southern California Regional NMR Facility (NSF Grant 7916324A1). We also thank Professor Peter B. Dervan and Peter G. Schultz for helpful discussions.

(14) See ref 1b, 5, and: Willcott, M. R.; Cargill, R. L.; Sears, A. B. *Prog. Phys. Org. Chem.* **1972**, *9*, 25-98.

(15) See ref 1b and: Cox, J. D.; Pilcher, G. "Thermochemistry of Organic and Organometallic Compounds"; Academic Press, New York, 1970. Turner, R. B.; Goebel, P.; Mallon, B. J.; Doering, W. von E.; Coburn, J. F., Jr.; Pomerantz, M. *J. Am. Chem. Soc.* **1968**, *90*, 4315-22.

(16) Kao, J.; Huang, T.-N. *J. Am. Chem. Soc.* **1979**, *101*, 5546-57.

Total Synthesis of (-)-Sarracenin by Photoannelation[1]

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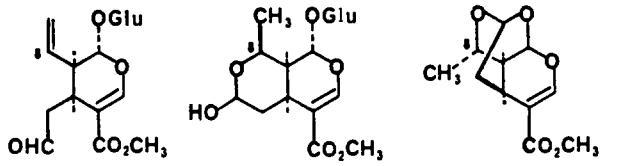
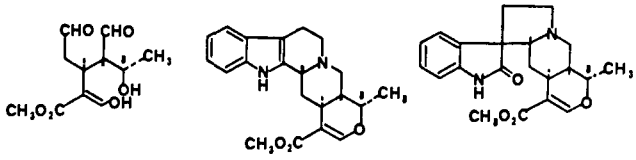
The secoiridoids such as secologanin (**1**) and moronoside (**2**) comprise a sizable subclass of the large group of natural products known as the iridoids.[2] These compounds are of interest primarily because of the demonstrated involvement of some of their members in the biosynthesis of several classes of alkaloids. In addition, some possess significant biological activity of their own.[3] The secoiridoids usually occur as glucosides although there are exceptions, a recent one being sarracenin (**3**), the total synthesis of which is the subject of this report.



1 **2** **3**

The isolation and single-crystal X-ray determination of sarracenin was reported in 1976 by Miles.[4] Sarracenin appears to be the same as the material derived from the emulsin (or acid) hydrolysis of morronoside (**2**) as previously reported by Souzu and Mitsuhashi,[5] although the discrepancy in the published specific rotations of the two samples (-68.8 vs. -35.6°) is bothersome.

Miles (among others) has made the observation that a suitably unraveled sarracenin, e.g., **4** (or **2**) is stereochemically disposed to be a convenient biosynthetic source of the nontryptophan 10-carbon portion of indole alkaloids such as ajmalicine (**5**) and mitraphylline (**6**) and perhaps others. The combination of bio-



4 **5** **6**

logical activity, biosynthetic interest, and unique molecular architecture make sarracenin an attractive target for synthesis, and in 1978 Whitesell and co-workers reported its preparation in 15 steps from 1,5-cyclooctadiene.[6] Described here is a seven-step total synthesis of racemic sarracenin as well as a synthesis of (-)-sarracenin which verifies that the absolute configuration of the natural material is as depicted.[7]

Logical retrosynthetic analysis suggests the following simple scheme for the synthesis of sarracenin involving first the photochemical addition of methyl diformylacetate (**9**) to a suitable alkene acetal, followed by dehydrative cyclization of the resultant bis hemiacetal to afford the natural product. Although this photochemical approach to other iridoids related to loganin has been previously employed by Büchi[8] and Uskokovic and Par-

(1) (a) Paper 8 in the series of photochemical annelations. Part 7: Baldwin, S. W.; Wilkinson, J. M. *J. Am. Chem. Soc.* **1980**, *102*, 3634. (b) Supported by the National Institutes of Health (GM 26266). (c) Presented in part at the 180th National Meeting of the American Chemical Society, Las Vegas, NV, Aug 25, 1980; Abstract No. ORGN 41.

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(3) Kubo, I.; Miura, I.; Nakanishi, K. *J. Am. Chem. Soc.* **1976**, *98*, 6704.

(4) Miles, D. H.; Kokpol, U.; Bhattacharyya, J.; Atwood, J. L.; Stone, K. E.; Bryson, T. A.; and Wilson, C. *J. Am. Chem. Soc.* **1976**, *98*, 1569.

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(6) Whitesell, J. K.; Matthews, R. S.; Helbling, A. M. *J. Org. Chem.* **1978**, *43*, 784.

(7) Biosynthetic considerations require that the absolute configuration of (-)-sarracenin be as depicted in **3**, with C-8 of the *S* configuration. This was assured by the laboratory conversion of natural morronside (**2**, *S* configuration) to sarracenin.[5]

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