intermolecular vibrational coupling.[10] However, in spite of the large temperature dependence of gauche concentration, the overall shape of the distribution curve is maintained.

The concentration of gauche bonds increases substantially toward the ends of the chain. This finding is at odds with the assumption of a more or less uniform distribution used in the interpretation of X-ray diffraction measurements on phase II.[11] In progressing away from the chain ends the number of gauche bonds decreases, reaching a minimum in the center that is about one-tenth the number at the ends. However, a substantial concentration of gauche bonds is observed in the middle of the chain so that our results conflict with those recently reported from an infrared study of n-C_{19} in phase II in which it was concluded that defects occur *only* at or near the ends.[12] We note that analogous gradients in conformational disorder have been previously inferred from NMR measurements on lipid bilayers in the liquid crystalline state,[3] and a variety of statistical models have been proposed to account for them.[13]

Acknowledgment. We gratefully acknowledge support from the National Institutes of Health and the National Science Foundation.

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cis-Azoalkanes. Mechanisms of Scission and Isomerization[1,2]

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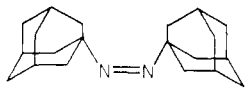
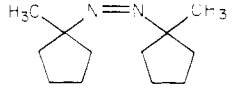
We propose, on the basis of pressure effects and solvent effects, that thermal decomposition of the symmetric *cis*-azoalkanes **1** and **2** proceeds via intermediate diazenyl radicals (Scheme I). This



1
(*cis*-azo-1-adamantane)



2
(*cis*-azo-1-methylcyclopentane)

scheme has been proposed by Porter for asymmetric arylalkyldiazenes,[3] but it has been generally accepted that **1** and other symmetric *cis*-azoalkanes isomerize (k_i) via inversion at nitrogen without radical formation[4,5a] and that symmetric azo compounds lose nitrogen (k_{N_2}) via simultaneous two-bond scission.[5]

We have previously shown[6] that "one-bond scission" initiators have *large* positive decomposition activation volumes[7] (ΔV_0^*: phenylazotriphenylmethane,[8a,b] +18 to +20 cm³/mol; *tert*-butylperbenzoate,[8c] + 12 cm³/mol) while "two-bond scission" initiators have *small* positive decomposition activation volumes[7] (ΔV_0^*: azocumene,[6e] +5 cm³/mol; di-*tert*-butylhyponitrite,[8d] +5 cm³/mol; *tert*-butylphenylperacetate,[8c] +2 cm³/mol). The activation volumes for deazatization ($\Delta V^*_{N_2}$) of **1** and **2** are consistent with one-bond scission (Figure 1, Table I).[9] Since these large positive values of $\Delta V^*_{N_2}$ show that recombination (k_{-1c}) of $RN_2{\cdot}R{\cdot}$ to give **1** or **2** competes with separative diffusion and β

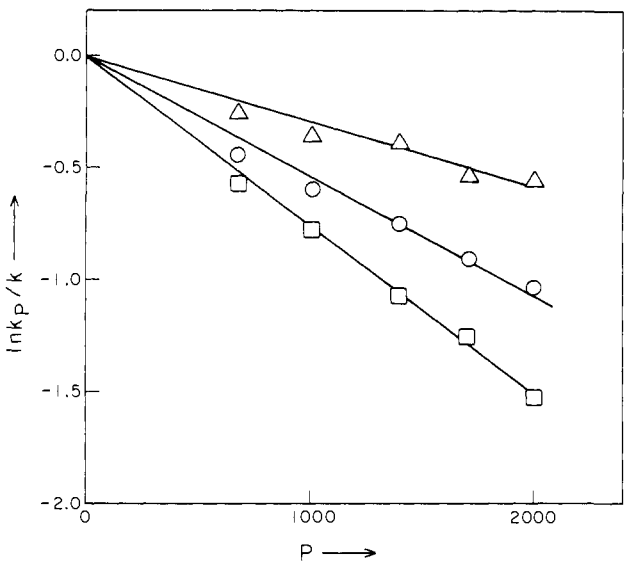


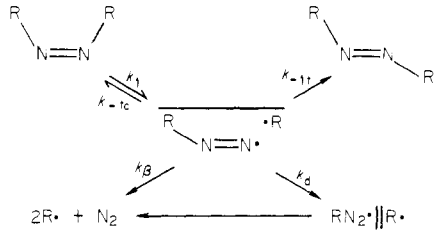
Figure 1. Pressure dependence of ln k_{N_2} (□), ln k_i (△), and ln k_0 (○) for decomposition of **1** in hexane (21.0 °C, 0.24 M *tert*-butylamine, degassed); k_0 is the observed decomposition rate constant for **1** and is equal to k_{N_2} + k_i (P in atm).

Table I. Activation Volumes for Deazatization and Isomerization of 1 and 2[a]

compd	solvent	T, °C	ΔV_0^*, cm³/mol	$\Delta V_{N_2}^*$, cm³/mol	ΔV_i^*, cm³/mol
1	hexane	21.0	+12	+18	+7
	EtOH	35.7	+7	(+28)[b]	+6
2	EtOH	9.0	+15	+17	(+9)[b]

[a] Calculated from the data by using the equation $\Delta V = -RT(\Delta \ln k/\Delta P)$.[7,9] [b] Unreliable because the particular reaction contributes little to the overall decomposition of the *cis*-azoalkane.

Scheme I



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(7) ΔV_0^* is derived from the pressure dependence of the observed decomposition rate constant k_0.
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(9) For **1** and **2**, $\Delta V^*_{N_2}$ and ΔV_i^* are the apparent activation volumes for deazatization (k_{N_2}) and isomerization (k_i), respectively; $k_0 = k_{N_2} + k_i$.

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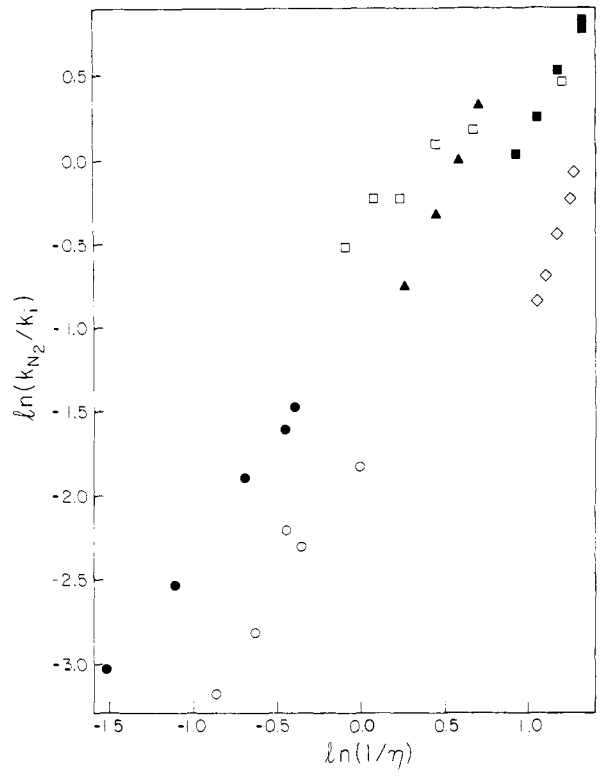

Figure 2. Viscosity dependence of ln (k_{N_2}/k_i); hexane (■), toluene (△), 2-propanol (●), acetone (◇), variable temperature;[4] hexane (□), ethanol (○), variable pressure.

scission,[10] recombination to give the stable trans isomers (k_{-1t}) should also be competitive.[11]

The smaller positive values of ΔV_i^* (Table I) are also consistent with this mechanism. On the basis of Scheme I, ΔV_i^* depends both on ΔV_1^* and the pressure dependences of the ratios k_{-1c}/k_{-1t} and k_{N_2}/k_i (eq 1).[12] The latter ratio decreases with increasing

$$\Delta V_i^* = \Delta V_1^* + RT\,(\partial \ln (1 + k_{-1c}/k_{-1t} + k_{N_2}/k_i)/\partial P) \quad (1)$$

pressure (Figure 1) while the ratio k_{-1c}/k_{-1t} is expected to remain constant or, perhaps, increase with pressure,[13] causing the differential term in eq 1 to be small. Thus, ΔV_i^* should be comparable to ΔV_1^* (ca. +5 cm^3/mol[10]), and this agrees with the data (Table I).[14] In contrast, Asano[15] has found that nonradical cis → trans isomerizations of azobenzenes give negative values of ΔV_i^*.

Decreases in k_{N_2}/k_i with increasing solvent polarity and decreasing temperature[4] have been explained in part by polar effects.[5,16] On the basis of Scheme I, k_{N_2}/k_i is equal to $(k_\beta + k_d)/k_{-1t}$, which is expected to decrease with solvent viscosity due to its effect on k_d. In fact, with the exception of the acetone data,[17] the values of ln (k_{N_2}/k_i), whether derived from *temperature variation*[4] in hexane, toluene, and 2-propanol or *pressure variation* in hexane and ethanol, show a rough linear correlation with ln $(1/\eta)$ (Figure 2),[18] consistent with our mechanism.

When diazenyl radicals are formed from *cis*-azoalkanes, we believe that they serve as isomerization intermediates (Scheme I).[19] However, not all *cis*-azoalkanes undergo deazatization (radical formation) competitively with isomerization.[4,5] In those cases, such as *cis*-azo-1-bicyclo[2.2.1]heptane and *cis*-azo-1-bicyclo[2.1.1]hexane, we agree that isomerization occurs by inversion at nitrogen. We also agree with Engel and Timberlake that increasing steric bulk of the R group increases the inversion rate.[4] However, we believe that isomerization via diazenyl radicals is a lower energy process for **1**, **2**, and the [2.2.2] isomer, for example, than isomerization via inversion.[20,21]

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Registry No. 1, 59388-63-5; **2**, 63561-19-3.

(10) See: Neuman, R. C., Jr.; Amrich, M. J., Jr. *J. Am. Chem. Soc.* **1972**, *94*, 2730.

(11) While recognized as a possible mechanism,[4] lack of evidence for diazenyl radical intermediates made it unattractive.

(12) Equation 1 is derived from Scheme I by recognizing that (a) $\Delta V_i^* = -RT(\partial \ln k_i/\partial P)$; (b) $\Delta V_1^* = -RT(\partial \ln k_1/\partial P)$; (c) $k_i = k_1[k_{-1i}/(k_{-1c} + k_{-1t} + k_d + k_\beta)]$; (d) $k_{N_2} + k_i[(k_\beta + k_d)/(k_{-1c} + k_{-1t} + k_d + k_\beta)]$, and (e) $k_{N_2}/k_i = (k_\beta + k_d)/k_{-1t}$.

(13) Geminate recombination to give *cis*-**1** or -**2** should be pressure accelerated. Formation of *trans*-**1** or -**2** (k_{-1t}) involves bond formation but also demands pressure-retarded rotational diffusion of the caged radicals.

(14) $\Delta V^*_{N_2} = \Delta V_1^* + RT(\partial \ln (1 + k_{-1c}/(k_\beta + k_d) + k_i/k_{N_2})/\partial P)$;[12] *both* rate constant ratios in this differential term *increase* with pressure causing $\Delta V^*_{N_2} \gg \Delta V^*_1$.[10]

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(17) The acetone data[4] are less accurate than those for the other solvents.

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(19) However, if $(k_\beta + k_d) \gg k_{-1t}$ (e.g. azo-2-methyl-2-propane), isomerization could be undetectable.[4,5]

(20) See ref 4, Figure 3; the log k_{rel} vs. E_s correlation could be fit with two lines, one through **1** and [2.2.2] and the other through [2.2.1] and [2.1.1].

(21) (a) Dannenberg[21b] calculates that *cis*-azoethane decomposes by one-bond scission: (b) Dannenberg, J., private communication.

An Incremental Approach to Hosts That Mimic Serine Proteases[1]

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The design and synthesis of enzyme-mimicking host compounds remains one of the challenging and stimulating problems of organic chemistry. We chose to study serine protease mimics because the structure and mechanism of action of these enzymes have been so thoroughly studied. Their active sites contain a complexing cavity, an acyl-receiving and -releasing hydroxymethylene group, and a proton-transfer system that is organized to complement the structures of certain amide and ester substrates.[2] The naturally occurring cyclodextrins neatly combine a complexing cavity with primary hydroxyl groups (nucleophiles), and they have been successfully modified to provide systems that exhibit some of the features of the serine proteases.[3]

The structures of two totally unknown systems, **1** and **2** (Chart I), have been designed with CPK molecular models to combine in a cooperative arrangement similar to that of the proteases a binding site, a primary hydroxyl, an imidazole, and a carboxyl group. These two "ultimate target" hosts have in common with simpler host **3** the same organization of binding site and hydroxyl nucleophile. We report here the synthesis of **3**, its binding

(1) We thank the Public Health Service for Grant GM 12640, which supported this research.

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