k_2,[2-4] $k_3/(k_{-1} - k_2)$ can be reduced to k_3/k_{-1} to a good approximation.[6]

Figure 1 shows a plot of log (k_3/k_{-1}) vs. σ^-.[7] The slope of the straight line gave the ρ for the (k_3/k_{-1}) of -1.48 ± 0.04. Since the ρ corresponding to k_{-1} was determined to be -0.08, the ρ for k_3 is -1.56 ($= -1.48 + (-0.08)$).[8] This quite large negative value shows that proton donation from the imidazolyl cation to the nitrogen atom of **1** is essentially complete in the transition state, whereas the bond between the carbonyl carbon atom and the nitrogen atom is almost intact. Thus, a large positive charge is located on the nitrogen atom in the transition state. k_3/k_{-1} in the hydrolysis of *m*-nitrotrifluoroacetanilide showed no D_2O solvent isotope effect (1.0 ± 0.2), which also indicates an almost complete proton transfer from the imidazolyl cation to the nitrogen atom of **1**.

The ρ for k_1 was determined to be $+0.57 \pm 0.06$ from the plot of log k_1 vs. σ^-. This value is slightly larger than the ρ obtained at 30 °C in ref 2 ($+0.42$). The k_1's in D_2O are 1.4 ± 0.2 times larger than those in H_2O, which support nucleophilic attack by hydroxide ion in this reaction. The nucleophilicity of deuteroxide ion is 20–40% higher than that of hydroxide ion.[9]

The rate constant of the reaction, in which the formation of **1** is followed by its rate-determining breakdown catalyzed by imidazolyl cation, is expressed by k_1k_3/k_{-1}. Thus, the ρ for this process is calculated to be -0.91 ($= -1.48 + 0.57$), using the ρ for k_1 ($+0.57$). This large *negative* ρ is consistent with the large *negative* ρ observed in the α-chymotrypsin-catalyzed hydrolyses of *N*-acetyl-L-tyrosine anilides (-1.8 at 35 °C).[1e] Furthermore, the magnitude of ρ for the present model reactions, observed at 70 °C, is quantitatively comparable with that in the enzymatic reactions, considering the known decrease of ρ with increasing temperature (-2.2 at 15 °C, -2.0 at 25 °C, and -1.8 at 35 °C).[1e]

On the other hand, the catalysis by neutral imidazole (k_4), which shows general base catalysis followed by water-catalyzed breakdown of the tetrahedral intermediate,[10] exhibited a *positive* ρ value of $+0.84 \pm 0.04$ (Figure 1). This value is close to the value for the reaction in which water catalyzes the breakdown of **1** ($+0.69$)[2,11] and is far different from the large *negative* ρ in the enzymatic reactions. Thus, the catalysis by water of the breakdown of the tetrahedral intermediate between Ser-195 and the anilide in the enzymatic hydrolyses of anilides is unlikely.

In conclusion, a large *negative* ρ was observed in the imidazolyl cation catalyzed breakdown of **1**, which is consistent with the finding in the enzymatic hydrolyses of anilides. The present result provides strong support for acid catalysis by the imidazolyl cation of His-57 rather than by water in the enzymatic hydrolyses of amides.

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Preparation and Decomposition of a Cis Cyclic Tetrazene, 1,4-Dimethyl-1,2,3,4-tetraaza-2-cycloheptene

Sir:

We report the preparation and the kinetics of the thermal decomposition of the title compound, **2**. This material was prepared in 18–25% yield by the oxidation of the dihydrazine **1**, using a modification of the procedure of Kreher and Wissman.[1]

1   2
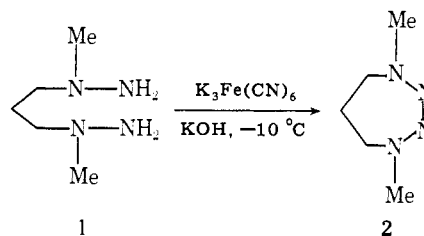
Acyclic tetraalkyl-2-tetrazenes have been shown to prefer the trans configuration.[2] No examples of cis acyclic tetraalkyltetrazenes are known, although Roberts and Ingold[3] suggested that photochemical decomposition of *trans*-tetrazenes involves initial trans → cis isomerization, followed by the dark (thermal) decomposition of the cis isomer. Nelsen and Fibiger,[4]
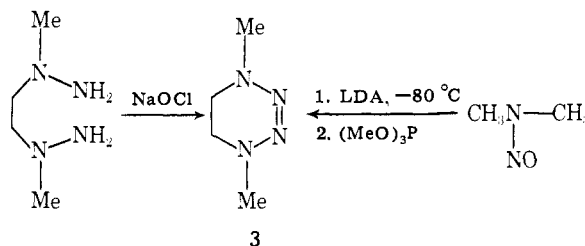

3

Table I. Thermolysis[a] of 1,4-Dimethyl-1,2,3,4-tetraaza-2-cycloheptene

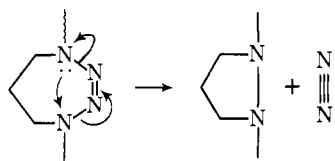| k, s^{-1} × 10^{-4} [b]	T, °C, ± 0.1°
1.76 ± 0.08	65
2.79 ± 0.1	70
4.66 ± 0.3	75
6.31 ± 0.5	80
13.05 ± 1.5	90
$\Delta H^\ddagger = 18.8 \pm 1$ kcal/mol, $\Delta S^\ddagger = -20.2 \pm 1$ eu	

[a] The reaction was carried out on 0.04 M **2** in *n*-hexadecane under nitrogen. The rate constants did not change when the concentration of **2** was doubled to 0.08 M. This indicates the absence of induced decomposition at this concentration range. [b] The rate constants are an average of three independent runs.

and then Seebach and co-workers,[5] prepared the first, authentic cis cyclic tetrazene, 1,4-dimethyl-1,4,5,6-hexahydro-1,2,3,4-tetrazine (**3**). Nelsen and Fibiger[4] studied the kinetics of the thermal decomposition of **3** and found, rather surprisingly, that it was relatively stable, ($\Delta H^{\ddagger}$ = 38 kcal/mol, $\Delta S^{\ddagger}$ = 17 eu). These values should be compared with those of tetramethyl-2-tetrazene, whose activation parameters in the gas phase were shown[6] to be $\Delta H^{\ddagger}$ = 36.1 kcal/mol, $\Delta S^{\ddagger}$ = 4.7 eu. Nelsen and Fibiger suggested that one possible explanation for this unexpected stability was the conformational restriction imposed by the cyclic structure, which increased the amino lone-pair interaction with the 2,3 bond. The larger ring size in
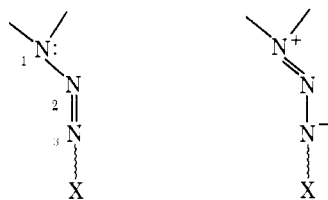

2, compared with that of **3**, might be expected to decrease the conformational rigidity of the cyclic *cis*-tetrazene, which would tend to decrease the lone-pair interaction. Thus it might be expected that **2** would decompose more readily than **3**. The data on the kinetics of the thermolysis of **2**, carried out by measuring the rate of nitrogen evolution in an automated, constant pressure device over the temperature range of 65–90 °C, are shown in Table I. The relative rate, $k(2)/k(3)$, at 90 °C is 8.8×10^4. These data demonstrate dramatically that, when the conformational restriction on the cis cyclic tetrazene is lifted, it becomes much less stable than the acyclic, *trans*-tetrazenes. In fact, the degree of the lowering of the enthalpy of activation in **2,** compared with that of tetramethyl-2-tetrazene ($\Delta\Delta H^{\ddagger} \approx 17$ kcal/mol) is much greater than would have been predicted on the basis of comparison with *cis*- and *trans*-azoalkanes ($\Delta\Delta H^{\ddagger} = 6$–8 kcal/mol).[4] Interestingly, Roberts and Ingold[3] reported that the putative *cis*-tetraisopropyl-2-tetrazene, which they suggested was the intermediate in the low temperature photolysis of the *trans*-tetrazene, decayed thermally with an activation energy of 24 ± 2 kcal/mol.

A surprising result of the rate study was the negative entropy of activation. Although some negative entropies for azoalkane thermolyses have been reported,[8] the present result was unexpected. The possibility that the reaction was catalyzed by mercury vapor (from the kinetics apparatus)[9] was not checked specifically, but other kinetic studies of tetrazene decompositions, using the same apparatus,[10] failed to reveal any abnormalities. Thus, assuming that our entropy of activation value is correct, two rationales can be offered. One is that the equilibrium conformation of the tetrazene is different from the optimum geometry for decomposition. Therefore, the entropy may reflect the preequilibrium step. The other rationale is that the decomposition does not go through a 1,5 biradical, but rather is a concerted process leading directly to N,N'-dimethylpyrrazoline and nitrogen. In keeping with this mecha-

nism, the product of the reaction is the pyrrazoline, in better than 90% yield. The present data, however, do not allow us to distinguish between these possibilities (or, indeed, additional ones).

A necessary component in the oxidation of the dihydrazine[11]
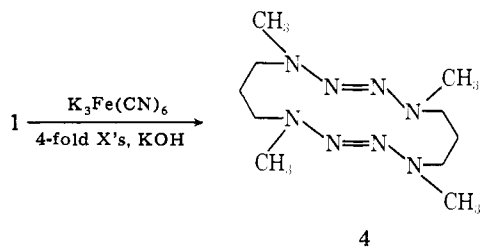
1 to the tetrazene **2** is a 20-fold excess of potassium hydroxide. When the amount of the base was lowered to a 4-fold excess, no **2** was formed; most of the reaction mixture consisted of intractable decomposition products. The workup of this mixture, however, did result in the isolation of small amounts (3–5%) of the solid, dimeric 14-membered-ring tetrazene, **4.** This material was analogous to the ditetrazene isolated by Nelsen and co-workers[12] in the oxidation N,N'-diamino-N,N'-dimethylethylenediamine. The ditetrazene **4** is completely stable and presumably has the trans,trans configuration.[13]

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Ion-Pair Equilibria in Cyclic 1,2-Semidiones[1]

Sir:

The alkali metal salts of 1,2-semidiones can exist as ion pairs even in solvents as polar as dimethyl sulfoxide (Me_2SO). For acyclic semidiones a mixture of cis ion-paired and trans free ion exists with sodium, potassium, or rubidium as the coun-