Mechanistic Characterization of the Intermediates in the Thermal and Photochemical Deazetation of Two Isomeric Methylenepyrazolines, 7-Isopropylidene-2,3-diazabicyclo[2.2.1]hept-2-ene and 2,2-Dimethyl-3,4-diazabicyclo[3.3.0]octa-3,8-diene. An Approach to the Generation and Capture of Protoplanar and Protobisected Trimethylenemethanes

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Abstract: The ΔS^{*} values (in gibbs/mol) for the thermal deazetations of 7-isopropylidene-2,3-diazabicyclo[2.2.1]hept-2-ene (**1**, 6.5 in benzene, 8.3 in CH_3CN) and 2,2-dimethyl-3,4-diazabicyclo[3.3.0]octa-3,8-diene (**2**, 8.1 in CH_3CN) are in the "normal" range for a thermal unimolecular fragmentation and are consistent with the chemical evidence that the deazetations lead directly to an interceptable singlet species rather than to the triplet ground state trimethylenemethane biradical. Rearrangement of **1** → **2** accompanies the thermolysis but not the photolysis of **1**. No rearrangement **2** → **1** is observed in the thermolysis of **2**. These phenomena are orbital symmetry effects ascribed to the phase properties of the C_s symmetric highest occupied molecular orbital of the singlet. The portion of the **1** that decomposes directly to the trappable singlet gives products that are indistinguishable from those obtained from **2**.

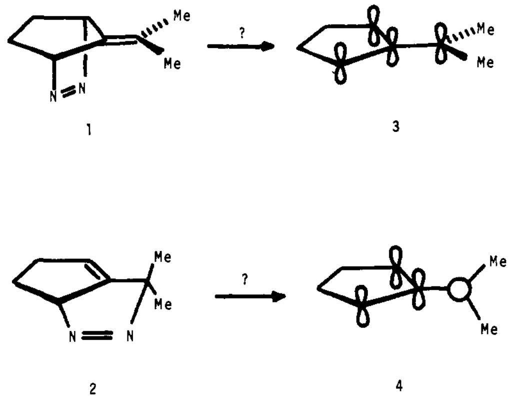
Much of the interest in the thermal and photochemical nitrogen extrusion reactions (deazetations) of 4-methylenepyrazolines[1-4] derives from the role of these substances as precursors of trimethylenemethane (TMM) biradicals. Theory[5] suggests that the *planar* TMM triplet should be the molecular ground state. Two singlets should lie at slightly higher energies, the more stable of them having a bisected geometry (a $^1B_1$ state in C_{2v} symmetry) and the less stable being planar ($^1A_1$). Since the energy separation between the two low-lying singlets is predicted to be small (2–6 kcal/mol), one is stimulated to inquire whether chemical behavior characteristic of each can be observed.

We planned to generate TMM species separately from protoplanar and protobisected compounds and to capture the intermediates with appropriate reagents. If the TMM biradicals preserved the traces of their origins for a period of time at least comparable to the characteristic capture time, it might be possible to observe different products from each.

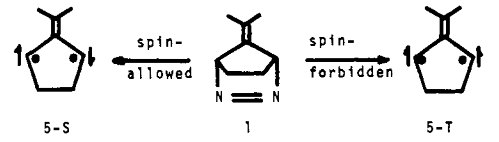
The present results show that intermolecular trapping is too slow to preserve any differences in behavior. Moreover, the observations help to elucidate spin correlation effects in the deazetations. We also have discovered a new thermal methylenepyrazoline rearrangement, which provides information on the question of simultaneity in the cleavage of the two C–N bonds of methylenepyrazolines.

The isomeric methylenepyrazolines, 7-isopropylidene-2,3-diazabicyclo[2.2.1]hept-2-ene (**1**) and 2,2-dimethyl-3,4-diazabicyclo[3.3.0]octa-3,8-diene (**2**), serve as the potential protoplanar and protobisected TMM precursors. Thus, one might imagine a spin-conservative departure of N_2 from **1** without any torsion about the exocyclic double bond to generate a planar singlet TMM **3**. The corresponding torsionless decomposition of **2**, accompanied by rehybridization of the isopropylidene carbon, would lead to a bisected species **4** (Scheme I).

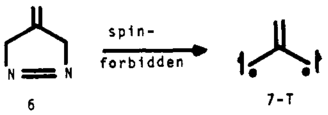
Scheme I



There are two potential pitfalls in this plan. First, if common products from the two diazenes are observed, they could arise from a common (e.g., stereoequilibrated) intermediate, or alternatively they might result from a rapid rearrangement which interconverts the diazenes *before* deazetation. Second, if the thermal decomposition of the diazenes **1** and/or **2** should occur by a *spin-forbidden* process leading directly to the triplet ground state[6-8] of the TMM, **5-T**, the composition of the products would provide misleading information on the nature of the singlet **5-S**.



In fact, a pioneering study by Crawford and Cameron[2a] reported exactly such a spin-forbidden thermal deazetation in the case of the parent compound 4-methylenepyrazoline (**6**), to triplet TMM itself (**7-T**).



We describe first a kinetic study which confirms the deductions[4,8] made earlier on other grounds that thermal decomposition

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[1] For a review, see: Engel, P. *Chem. Rev.*, **1980**, *80*, 99.

[2] (a) Crawford, R. J.; Cameron, D. M. *J. Am. Chem. Soc.* **1966**, *88*, 2589. (b) Crawford, R. J.; Mishra, A. *Ibid.* **1966**, *88*, 3963.

[3] Dowd, P. *Acc. Chem. Res.* **1972**, *5*, 242.

[4] Berson, J. A. *Acc. Chem. Res.* **1978**, *11*, 446.

[5] For a review, see: Borden, W. T.; Davidson, E. R. *Annu. Rev. Phys. Chem.* **1978**, *30*, 125.

[6] Platz, M. S.; McBride, J. M.; Little, R. D.; Harrison, J. J.; Shaw, A.; Potter, S. E.; Berson, J. A. *J. Am. Chem. Soc.* **1976**, *98*, 5725.

[7] (a) Berson, J. A.; Duncan, C. D.; Corwin, L. R. *J. Am. Chem. Soc.* **1974**, *96*, 6175. (b) Berson, J. A.; Corwin, L. R.; Davis J. H. *Ibid.* **1974**, *96*, 6177.

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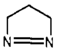
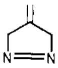
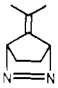
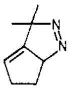
Table I. Activation Parameters for Thermal Decomposition of Diazenes[e]

	compd	E_a, kcal/mol	A, s^{-1}	$\Delta S^{\ddagger}$, gibbs/mol	ref
8		42.4	9.5×10^{15}	11.2	2b
9		37.3	9.5×10^{14}	8.7	2b, 10
6		32.6	2×10^{13}	−1.1	2a
1		$27.6^{a,b}$ $28.8^{a,c}$	5×10^{14} 1×10^{15}	6.5^d 8.3^d	this work this work
2		$28.0^{a,c}$	9.5×10^{14}	8.1^d	this work

[a] Estimated error ±0.5 kcal/mol. [b] In benzene solvent. [c] In acetonitrile solvent. [d] Estimated error ±1 gibbs/mol. [e] Literature values refer to reactions in the gas phase.

of diazenes **1** and **2** are spin-allowed processes. The search for the thermal diazene → diazene rearrangement is reported later.

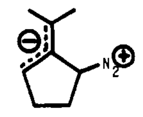
Results

Kinetics of the Thermal Deazetations of 1 and 2.[9] The principal experimental evidence offered[2a] in favor of the direct **6** → **7**-T reaction was the observed entropy of activation, $\Delta S^{*} = -1.1$ gibbs/mol, which was about 12 gibbs/mol more negative than that found for pyrazoline.[2b] Since our studies[7,8] of the products of cycloadditions had strongly suggested that the proximate hydrocarbon intermediate in the thermal deazetation of **1** was an interceptable *singlet* species which only subsequently crossed over to the triplet, a discrepancy in behavior between the diazenes **1** and **6** became apparent. The criteria of mechanism that had been applied to the two cases were different, however, and it seemed desirable to investigate these systems further by a common test, either a product study of cycloadditions of **7** or a kinetic study of the thermal deazetation of **1**.

As summarized elsewhere,[4] the application of intermolecular cycloaddition product studies to the parent TMM **7** does not seem to be practical since the intramolecular cyclization of this intermediate to methylenecyclopropane is efficient and irreversible. Accordingly, we decided to obtain the activation parameters of the thermal decomposition of diazenes **1** and **2** for comparison with those observed[2a] for the corresponding reaction of diazene **6**.

The decomposition of the diazenes can be monitored by analysis for *unreacted* **1** or **2**. A sample of the starting or partially decomposed diazene solution is inserted into the injector port of a gas chromatograph (GC) at 230 °C. The substance quickly liberates its nitrogen, which is estimated by GC peak area, using a molecular sieves column. For both **1** and **2**, good first-order kinetics are observed through at least 3 reaction half-lives. Table I summarizes the Arrhenius parameters and ΔS^{*} values for these two substances and also for **6** and two other model pyrazolines.

The effect of solvent polarity (expressed as dielectric constant) on the rate of decomposition of diazene **1** is negligible. In benzene ($D = 2.27$) or acetonitrile ($D = 36.2$), the rates and activation parameters show no significant differences (Table I). There seems to be no reason to postulate zwitterionic intermediates, e.g., **10**, in the rate-determining step, since the reaction in acetonitrile should have been much accelerated.[11]



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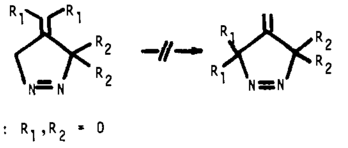
As we show later, only about 70% of the thermal deazetation of **1** proceeds directly. The remaining 30% goes by an indirect pathway in which **1** first arranges to the isomeric diazene **2**, which loses nitrogen independently. The reverse reaction **2** → **1** seems to be of negligible significance under these conditions. Thus, although the Arrhenius parameters of Table I may be taken at face value for diazene **2**, they require some interpretation in the case of **1**, where they represent a blend of a true deazetation E_a and A for 70% of the N_2-generating process with an *apparent* E_a and A for the remaining 30%. The latter values are not well defined because there is no clear-cut rate-determining step in the indirect mechanism, but, since the Arrhenius values for **2** do not differ significantly from those of **1**, and since there are no obvious reasons to expect drastically different values for the rearrangement step, we adopt the observed E_a and A values for **1** as those associated with deazetation.

The activation energy terms, E_a, show some regularities. Thus, incorporation of the pyrazoline unit in a bridged bicyclic system lowers E_a by about 5 kcal/mol in both the parent series (compare **9** vs. **8**) and in the methylenepyrazolines (compare **1** vs. **6**), presumably in part because of approximately equal increments of strain energy released in the transition states of the bicyclic reactants, **9** and **1**. This ground state destabilization effect should operate regardless of whether the two C–N bonds cleave sequentially or simultaneously. For this reason, the observed constancy of the E_a increment in the two series cannot be taken as indicative of a constant mechanism.

The effect of conjugation again seems to be roughly constant. Introduction of an exocyclic double bond in the 4 position of the pyrazoline lowers E_a by about 10 kcal/mol in both the monocyclic (compare **8** vs. **6**) and bridged bicyclic (compare **9** vs. **1**) series. It is tempting to ascribe this to the stabilization of the deazetation transition state by incipient TMM resonance, but the interpretation is clouded by the observations reported below which suggest a sequential cleavage of the C–N bonds of **1**. If the first of these bond cleavages is rate determining, the transition state could be stabilized by incipient allylic rather than trimethylenemethanic resonance. The observed value of 10 kcal/mol would not be inconsistent with this interpretation.[12,13]

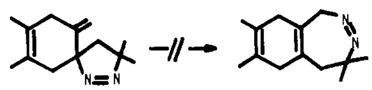
The ΔS^{*} terms for deazetation of the bicyclic methylenepyrazolines **1** and **2** are strongly positive and are comparable in magnitude to those of the pyrazolines **8** and **9** which lack the exocyclic methylene group. This finding contrasts with the case of the monocyclic methylenepyrazoline **6**,[2a] in which ΔS^{*} is much more negative.

The Diazene–Diazene Rearrangement, 1 → 2. Previous careful searches have shown that diazene–diazene rearrangements do not accompany the thermal deazetations of the methylenepyrazolines **11a,b**[14] nor of the spirodiazene **12**.[15] On the other hand, allylic



11a: $R_1, R_2 = O$

b: $R_1 = H, R_2 = Me$



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(8) Corwin, L. R.; McDaniel, D. M.; Bushby, R. J.; Berson, J. A. *J. Am. Chem. Soc.* **1980**, *102*, 276.

(9) For preliminary communications see: (a) Berson, J. A.; Duncan, C. D.; O'Connell, G. C.; Platz, M. S. *J. Am. Chem. Soc.* **1976**, *98*, 2358. (b) Cichra, D.; Platz, M. S.; Berson, J. A. *Ibid.* **1977**, *99*, 8507.

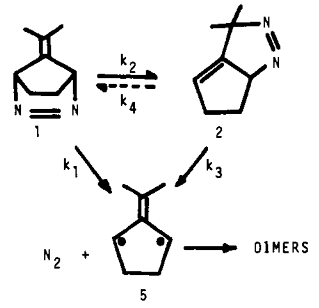
(10) Cohen, S. G.; Zand, R.; Steel, C. *J. Am. Chem. Soc.* **1961**, *83*, 2895.

(11) (a) Reichardt, C. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 29. (b) Kosower, E. J. "An Introduction to Physical Organic Chemistry"; Wiley: New York, 1968; p 259 ff.

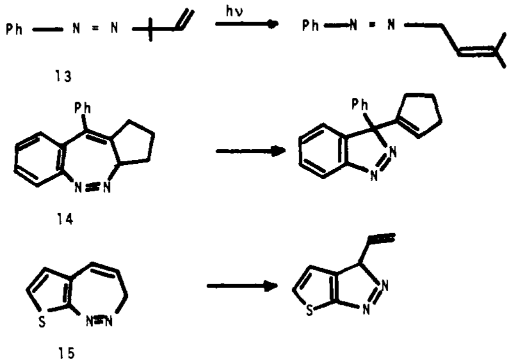
(12) Egger, K. W.; Golden, D. M.; Benson, S. W. *J. Am. Chem. Soc.* **1964**, *86*, 5420.

(13) Doering, W. von E.; Beasley, G. H. *Tetrahedron* **1973**, *29*, 2231.

Scheme II



rearrangements do occur in the photodeazetation of **13**[16] and in the thermolysis of **14**[17] and **15**.[18]



By the kinetic techniques already described, we find that the total first-order rate constant for deazetation of an acetonitrile solution of pure bridged diazene **1** at 50.0 °C is 4.96 × 10^{-5} s^{-1}, and that for fused diazene **2** is 7.34 × 10^{-5} s^{-1}. These facts permit a linear consecutive scheme **1** → **2** → products, but exclude the alternative **2** → **1** → products as the sole mechanism of deazetation since the latter pathway would not account for the observed relative deazetation rates **2** > **1**.

The detection of the **1** → **2** rearrangement is difficult by ordinary NMR spectroscopy, because of the close correspondence of the chemical shifts of the two isomers. However, in $CDCl_3$ solutions, tris(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionato)europium ($Eu(fod)_3$), which is known[19] to complex with cis diazenes, produces different pseudocontact shifts for the methyl signals of **1** and for the nonequivalent methyl signals of **2**. This permits quantitative analysis of the **1**/**2** ratio in the diazenes recovered by chromatography after partial pyrolysis.

Starting from pure **1** (**1**/**2** ratio ≥20), the **1**/**2** ratio in the recovered diazene declines over time to a value of 2.5 after 8.5 h (82% conversion to deazetation products). Since it is already known that deazetation of fused diazene **2** is *faster* than that of bridged diazene **1** under these conditions, the decrease in the **1**/**2** ratio over time cannot be attributed to concentration of an originally indetectably small amount of **2** in the starting material by selective decomposition of **1**. The most reasonable interpretation is that **1** → **2** rearrangement accompanies the deazetation.

In the reaction starting with the fused diazene **2**, it is not so easy to test for diazene–diazene rearrangement. The deazetation of the rearrangement product, bridged diazene **1**, is *slower* than that of **2**. Moreover, it is difficult to obtain **2** absolutely free of **1** by synthesis (our best samples were about 93% **2** and 7% **1**). Therefore, the **1**/**2** ratio in a partially decomposed sample of **2** necessarily would be higher than that at the beginning of the reaction, regardless of whether the **2** → **1** rearrangement occurs during deazetation. A more quantitative test for rearrangement requires a kinetic analysis of the three-component system, **1**, **2**, and the deazetation products, which are the dimers of the TMM diyl species **5**.

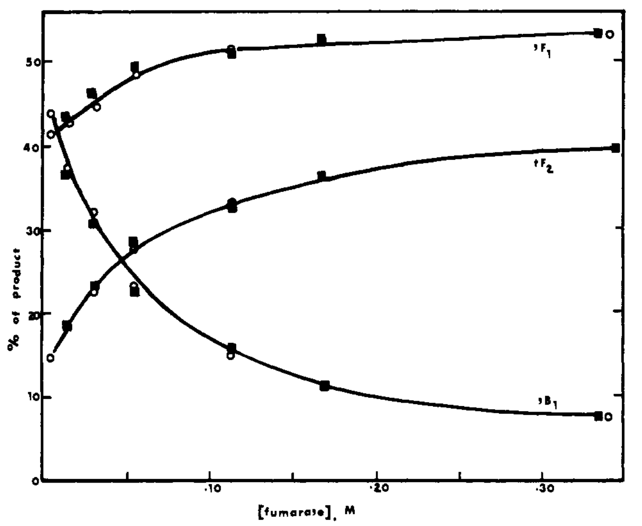


Figure 1. Products from the thermal decomposition of the fused diazenes **2** and **3** in the presence of varying concentrations of dimethyl fumarate in CH_3CN solution at 60 °C. The data points from **2** and **3** are circles and squares, respectively. Curves tF_1 and tF_2 represent products of fused structure F with the trans carbomethoxy configuration.[15,16] Curve tB_1 represents the bridged adduct B of trans configuration. Bridged cis product can be detected but constitutes <2% of the total in these experiments.

The kinetic behavior can be fitted to the triangular mechanism of Scheme II with rate constants determined by a computer-assisted Runge–Kutta numerical integration of the differential equations. An internally consistent set of rate constants that fits the observed data for the concentration of **1**, **2**, and products (dimers of the biradical **5**) has the values (×10^5 s) k_1 = 3.50, k_2 = 1.50, k_3 = 7.35, and k_4 = 0. The root mean square (rms) errors for the fit to the three concentration values are 0.023, 0.029, and 0.031 from the pyrolysis of **1** (Figure 1) and 0.009, 0.009, and 0.001 from the pyrolysis of **2**.

Even though the interactive computer program we use for curve fitting does not provide rigorous estimates of the "best" values of the rate constants, the conclusion that k_4, the rate constant for the reverse rearrangement, **2** → **1**, is small seems reasonably well established. For example, we find empirically that attempts to use the same k_1, k_2, and k_3 values as before in combination with k_4 = 3.0 × $10^{-6}$$s^{-1}$, about 20% k_2, markedly increase the rms errors for the reaction starting from **2**.

Further evidence that is consistent with a small value for k_4 may be obtained by two other comparisons. In Scheme II, if k_4 = 0, the disappearance of total diazene in the pyrolysis of **2** would be a simple first-order reaction with rate constant k_3. Experimentally, this reaction obeys first-order kinetics with a rate constant (7.34 ± 0.2) × 10^{-5} s^{-1}, which agrees exactly with the computer-fitted value of k_3. Moreover, in the reaction starting from bridged diazene **1**, the rate law when k_4 = 0 reduces to the integrated form[20]

$$-\ln([1]/[1_0]) = (k_1 + k_2)t \qquad (1)$$

which predicts that the disappearance of **1** also should be first order. This is again in agreement with experiment, the observed rate constant 4.96 × $10^{-5}$$s^{-1}$ being very close to the sum $k_1 + k_2$ = 5.00 × 10^{-5} s^{-1} obtained by numerical integration.

Evidently, the bridged → fused rearrangement, **1** → **2**, is essentially irreversible under these conditions. We can obtain a lower

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(14) Crawford, R. J.; Cameron, D. M.; Tokunaga, H. *Can. J. Chem.* **1974**, *52*, 4025.

(15) McBride, J. M.; Karch, N., unpublished work; Karch, N. Ph.D. Thesis, Yale University, 1973.

(16) (a) Porter, N. A.; Marnett, L. J. *J. Am. Chem. Soc.* **1973**, *95*, 4361. (b) Porter, N. A.; Iloff, P. M., Jr. *Chem. Commun.* **1971**, 1575.

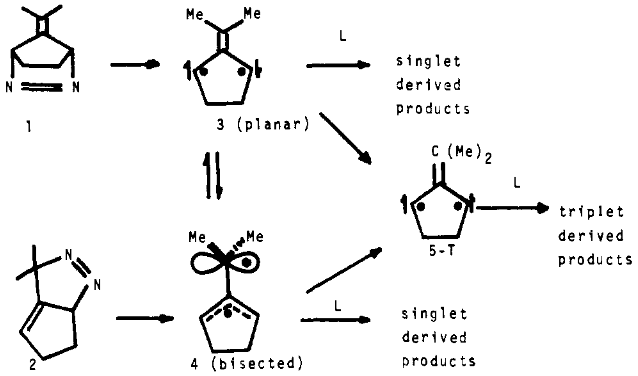
(17) Done, J. N.; Knox, J. H.; McEwan, R.; Sharp, J. T. *J. Chem. Soc., Chem. Commun.* **1974**, 532.

(18) Tsuchiya, T.; Enkaku, M.; Sawanishi, H. *J. Chem. Soc., Chem. Commun.* **1978**, 568.

(19) Bergman, R. G.; Keppel. R. A. *J. Am. Chem. Soc.* **1972**, *94*, 1350.

(20) Cf. Alberty, R. A.; Miller, W. G. *J. Chem. Phys.* **1957**, *26*, 1231.

Scheme III



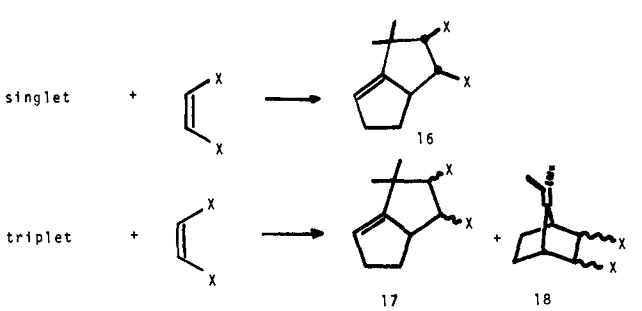
limit for the standard free energy difference between the isomeric diazenes by assuming the ratio $k_4/k_2 \leq 0.2$ implied by the kinetic analysis above. On this basis, the bridged isomer **1** is less stable than the fused one **2** by $\Delta G° \geq 1040$ cal/mol.

The thermal deazetation of bridged diazene **1** thus proceeds by two competing pathways. One is a direct decomposition to reactive intermediates. The other is indirect via fused diazene **2**. In the trapping studies described below, the chemistry of Scheme II is modified because the reactive intermediate, diyl **5**, forms cycloadducts rather than dimers. We may calculate the portion of the cycloadducts (or dimers) formed from the **5** generated in the direct pathway as $100[k_1/(k_1 + k_2)] = 70\%$. The major deazetation pathway from **1** therefore is independent of that from **2**, that is, **1** → **2** rearrangement is not fast enough to ensure an identical mixture of trapping products from the two isomers.

In contrast to the thermal decomposition, photochemical deazetation at 350 nm and 0 °C of CH_3CN solutions of **1** is not accompanied by rearrangement to **2**. The bridged diazene can be recovered from 15 runs representing increasing extents of partial photolysis (7–99% reaction), but no rearrangment to the fused isomer can be detected. This finding is in agreement with the high quantum yield of 0.95 ± 0.05 for the photodeazetation of **1**.[21] Here also, the deazetations are largely independent.

Products of the Thermal and Photochemical Deazetations of 1 and 2. Having established the independence of the main deazetation pathways of **1** and **2**, we are at last ready to ask whether there is a detectable difference in the cycloaddition chemistry of the singlet intermediates.

The cascade mechanism diazene → singlet → triplet causes a dilution effect,[7,8] in which the products characteristic of singlet cycloaddition (regiospecifically fused and stereospecifically syn, e.g., **16**) are favored at high concentration but are gradually rivalled in importance by the triplet products (regiorandomly and stereorandomly bridged and fused, syn and anti, e.g., **17** and **18**).



If two distinct singlets are formed from **1** and **2** (Scheme III), it is conceivable that they may display differences not only in their distribution to cycloaddition products but also in their rates of intersystem crossing (isc) to triplets. The probability of isc might be higher in a nonplanar than in a planar singlet.[22] Therefore, unless geometric planar–bisected interconversion (**3** ⇌ **4**) is fast, the reaction mixture from **2** and a given concentration of trapping olefin will be richer in triplet-derived products than that from **1**.

We now have studied the thermal deazetations of **1** and **2** in the presence of two of the most reactive[4,8,23] traps for the singlet diyl, dimethyl fumarate and fumaronitrile. At sufficient concentration, these substances intercept the singlet from **1** with high efficiency and virtually shut off isc to the triplet TMM.

In several comparisons, we find that the product compositions from thermal deazetations of diazenes **1** and **2** are identical throughout the practical range of trapping agent concentrations. For the case of dimethyl fumarate in the range 0.007–0.350 M in CH_3CN, there is a pronounced dilution effect (Figure 1), but within experimental error the distributions of products are independent of the diazene. Similarly, thermal deazetations of **1** and **2** give identical mixtures of cycloadducts in 0.2–4.12 M fumaronitrile.

We also find no difference in behavior in the photochemical deazetations of **1** and **2**. Because of the known[9a,21] temperature effect on the product composition from **1**, the distribution of products from the photochemical reactions (run at 0 °C) is not the same as that from thermolysis (run at 60 °C), but photolysis of **1** gives the same distribution as that of **2**.

Discussion

Geometry of the Singlet Intermediates. The **1** ⇌ **2** rearrangement before deazetation accounts for only a minor part of the equivalence of the product compositions, which therefore must result from the nature of the diyls themselves. Any distinction in structure between the singlet intermediates from the protoplanar and protobisected precursors **1** and **2** either fortuitously fails to result in distinctive reactivities or, more plausibly, is lost during the lifetime of the intermediates.

The most reasonable mechanism for the functional equivalence of the intermediates from **1** and **2** is the interconversion of the planar and bisected species **3** and **4** by torsion about the exocyclic bond. Similar processes have been considered[24-26] as likely mechanisms for the loss of stereochemical integrity of the isotopic label in the photolysis at −78 °C of the diazene **19**, which gives partially scrambled **20** and **21**. Complete thermal scrambling in this system (**20** ⇌ **21**) occurs at −40 °C and in the rearrangement **22** → **23** at −30 °C.

If the rotational barrier for planar–bisected interconversion in the singlet TMM were as high as 6 kcal/mol, the trapping rate constant would have to be about $4.5 \times 10^8\ s^{-1}$ for 50% preservation of the original geometry. This rate at 1 M olefin is about 10% of the diffusion-controlled encounter frequency under our conditions and hence achievable in principle. However, if the rotational barrier were as low as 2 kcal/mol, as is suggested by our recent studies of a related system,[24-26] the trapping rate would have to be about two to three orders of magnitude larger than the encounter frequency to preserve a distinction in products from **1** and **2**. Nevertheless, it is conceivable that different methods of generating the singlet species **5** could yet demonstrate independent identities for the planar and bisected forms.

Mechanism of the Deazetation. The experiments illuminate several reactivity patterns that call for explanation: (1) thermal deazetations of the bridged diazene **1** and the methylenepyrazoline **6** show striking differences in their entropies of activation, with that of **6** being much more negative; (2) thermal but not photochemical deazetation of **1** is accompanied by rearrangement to

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[21] Platz, M. S.; Kelsey, D. R.; Berson, J. A.; Turro, N. J.; Mirbach, M. *J. Am. Chem. Soc.* **1977**, *99*, 2009.

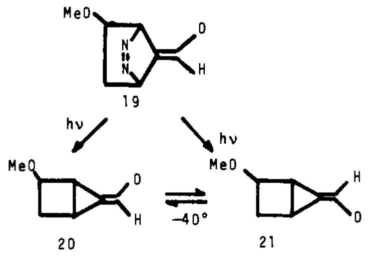
[22] For discussions of geometric factors in isc, see: (a) McGlynn, S. P.; Smith, F. J.; Cilento, G. *Photochem. Photobiol.* **1964**, *3*, 269. (b) McGlynn, S. P.; Azumi, T.; Kinoshita, M. "Molecular Spectroscopy of the Triplet State"; Prentice Hall: Englewood Cliffs, N.J., 1969; Chapter 5; (c) Salem, L.; Rowland, C. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 92. (d) Turro, N. J. "Modern Molecular Photochemistry"; Benjamin/Cummings: Menlo Park, Calif., 1978; pp 48–51, 164–170.

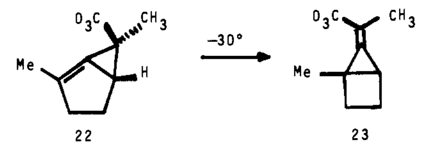
[23] Duncan, C. D.; Corwin, L. R.; Davis, J. H.; Berson, J. A. *J. Am. Chem. Soc.*, **1980**, *102*, 2350.

[24] Lazzara, M. G.; Harrison, J. J.; Rule, M.; Berson, J. A. *J. Am. Chem. Soc.* **1979**, *101*, 7092.

[25] Salinaro, R. F.; Berson, J. A. *J. Am. Chem. Soc.* **1979**, *101*, 7094.

[26] Lazzara, M. G.; Harrison, J. J.; Berson, J. A., paper in preparation.



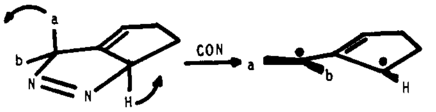


2; (3) no rearrangement is observed[14] in the thermal deazetation of the simple methylenepyrazolines **11**.

With regard to point (1), Duncan, Halevi, and Trindle[27] have presented theoretical reasons why the probability of a Landau–Zener singlet–triplet crossing during thermal extrusion of nitrogen from the acyclic methylenepyrazoline **6** would be favored by a conrotation of the two ring methylene groups. Cleavage of both C–N bonds in a concerted decomposition of **6** then could lead to singlet N_2 and *triplet* TMM as the proximate products. RRKM calculations[27] of the Arrhenius parameters for the direct **6** → triplet TMM reaction gave an *A* value about two orders of magnitude lower than that calculated for the **6** → singlet TMM pathway. Crawford and Cameron's finding[2a] of a value between these extremes was compatible with a mixture of spin-conservative and spin-forbidden reactions.

Since conrotation of the bridgehead carbons during deazetation of the bridged bicyclic diazene **1** is sterically prohibited, this mechanism for facilitation of the spin-forbidden diazene → triplet TMM pathway is not available in that case. The hypothesis[27] that spin-conservative decomposition then dominates, of course, is in accord with a body of experimental evidence[4,8] demonstrative of the singlet nature of the first-formed intermediate and with the present finding of a normal $\Delta S^‡$.

It does not necessarily follow, however, that all sterically uninhibited 4-methylenepyrazolines will decompose in a direct conrotatory reaction to the triplet. A case in point is diazene **2**, deazetation of which could be imagined to occur by an unrestricted conrotatory process, viz.,

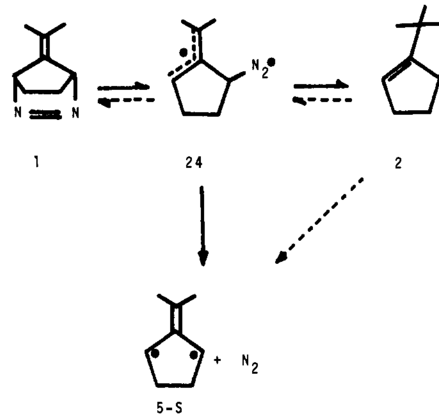


2

We do not know whether deazetation of **2** is conrotatory, but, in any case, the formation of *singlet* TMM in the thermal deazetation (described above) and the positive $\Delta S^‡$ (Table I) argue strongly against a direct **2** → triplet TMM reaction. It seems likely that subtle structural factors may shift the balance of the competing triplet-forming and singlet-forming pathways in methylenepyrazoline deazetations. Further theoretical and experimental exploration of this interplay would be valuable.

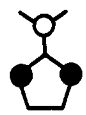
We believe that orbital symmetry constraints provide the most plausible explanation for points (2) and (3). Although it is possible that the deazetation of bridged diazene **1** and its rearrangement to fused diazene **2** occur by completely distinct pathways, the most economical mechanism (Scheme IV) involves the common intermediate singlet diazenyl biradical **24**, formed by cleavage of only one of the two C–N bonds. Loss of N_2 from **24** generates the singlet diyl **5-S**, but a fraction of the diazenyl biradicals can recyclize at the alternative site to give the rearranged diazene **2**.

Scheme IV



An alternative rearrangement pathway might involve cleavage of *both* C–N bonds followed by recapture of molecular nitrogen by the biradical. If this mechanism prevailed, the photochemically produced diyl, whose properties suggest[9,21] that it is the same as the thermally generated one, also should recapture N_2. Since no rearrangement **1** → **2** is observed in the photodeazetation, the dissociation–recombination pathway for the thermal rearrangment seems improbable.[28]

A hypothetical concerted two-bond deazetation of **1** directly to **5-S** and N_2 is, in a formal sense, the reverse of the addition of an olefin to **5-S** to give a *bridged* cycloadduct. Such cycloadditions are very unfavorable relative to those leading to fused adducts.[4,7,8,29] This regiospecificity is now rationalized[29] as an orbital symmetry effect, which in the present case is most simply modeled by the frontier orbital approximation, using the hypothesis that the highest occupied molecular orbital (HOMO) of planar **5-S** is the C_s symmetric component (**25**) of the nominally degenerate TMM nonbonding pair of π MOs. Concerted thermal decomposition of *bridged* diazene **1** to a singlet with a symmetric HOMO is orbital symmetry forbidden because of the mismatch of the phases of **25** and the N_2 π^* orbital.



25

On the other hand, in the photodeazetation of **1**, the orbital symmetry requirements appropriate to the ground-state reaction no longer apply. Although the precise excited state involved has not been identified, the observed absence of rearrangement, which suggests a concerted two-bond cleavage, is not surprising.

It will be noted that the thermal deazetation of *fused* diazene **2** to the same singlet intermediate is orbitally symmetry allowed, since the side-chain and ring positions of the TMM HOMO are out of phase and therefore match the symmetry of the N_2 π^* orbital. Whether the deazetation of **2** is truly concerted is not yet clear, but at least one criterion of concert is satisfied: no rearrangement **2** → **1** is observed in the thermal deazetation.[30]

Conclusions

Thermal deazetations of the bridged and fused diazenes **1** and **2** show no kinetic evidence of a spin-correlation effect. The $\Delta S^‡$ terms are "normal", in accord with the chemical evidence that the first interceptable intermediate is a singlet biradical. Thermal deazetation of **1** is accompanied by rearrangment to **2**, but no

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[27] Duncan, C. D.; Halevi, E. A.; Trindle, C. *J. Am. Chem. Soc.* **1979**, *101*, 2269.

[28] We thank Professor J. M. McBride for this insight.

[29] (a) As usual[29b,c] we mention the possibility that the role of **5-S** may be played, for orbital symmetry purposes, by 5-isopropylidenebicyclo[2.1.0]-pentane. (b) Siemionko, R.; Shaw, A.; O'Connell, G. C.; Little, R. D.; Carpenter, B. K; Shen, L.; Berson, J. A. *Tetrahedron Lett.* **1978**, 3529. (c) Siemionko, R. K.; Berson, J. A. *J. Am. Chem. Soc.* **1980**, *102*, 3870.

[30] This is not decisive, since the failure to find rearrangement could be caused by a slow ring closure of the diyl, **24** → **1**, rather than by a fast concerted decomposition, **2** → **5-S**.

rearrangement is observed in the thermal deazetation of **2** or in the photodeazetation of **1**. These phenomena are orbital symmetry effects. The chemical behaviors of the singlet diyls generated from protoplanar and protobisected precursors **1** and **2** are indistinguishable by the trapping techniques used so far.

Experimental Section

Instruments and standard procedures follow those described elsewhere.[8] The analytical GC columns used were those designated[8] as columns A–E.

***N*,*N*-Dicarbomethoxy-3,4-diaza-2,2-dimethylbicyclo[3.3.0]oct-8-ene.** To 10 mL of dimethyl azodicarboxylate was added 0.9 g of 7-isopropylidene-2,3-diazabicyclo[2.2.1]hept-2-ene.[8] The mixture was heated under nitrogen at 40–45 °C for 3–4 days and then at 60 °C overnight. The mixture was cooled to room temperature and dissolved in 120 mL of ether. After the mixture was cooled to dry ice–acetone temperature, 24 mL of hydrazine hydrate (80% aqueous solution) was added with stirring at dry ice–acetone temperature for 30 min, then another 24 mL of hydrazine hydrate was added. The solution was allowed to warm to room temperature, after which it was poured into a separatory funnel. Water was added and the layers were separated. The aqueous layer was extracted with ether and the combined organic layers were dried over anhydrous magnesium sulfate. The solvent was removed on the rotary evaporator to give 2.09 g of fused carbamate containing some dicarbomethoxyhydrazine.

The fused carbamate can be purified[31] by GC on a 2 ft × $^3/_8$ in. 25% Carbowax 20M column at 140 °C. NMR ($CDCl_3$): δ 1.3 (s, 3 H, CH_3), 1.7 (s, 3 H, CH_3), 1.6–2.25 (m, 1 H), 2.3–2.7 (m, 3 H), 3.65 (s, 3 H, CO_2CH_3), 3.75 (s, 3 H, CO_2CH_3), 4.75 (m, 1 H, CHN), 5.55 (m, 1 H, olefinic).

Anal. Calcd for $C_{12}H_{18}O_4N_2$: C, 56.67; H, 7.15; N, 11.02. Found: C, 56.61; H, 7.12; N, 11.20.

3,4-Diaza-2,2-dimethylbicyclo[3.3.0]octa-2,2-diene. *N*,*N*-Dicarbomethoxy-3,4-diaza-2,2-dimethylbicyclo[3.3.0]oct-8-ene (1.64 g) in 25 mL of degassed ethylene glycol was added with stirring under nitrogen to 5 g of potassium hydroxide in 20 mL of ethylene glycol at 125 °C. The solution was stirred at 125 °C for 30 min and then cooled to room temperature. A small amount of ice and water was added and the solution was acidified with dilute hydrochloric acid. The solution was heated to 40 °C and then neutralized with ammonium hydroxide (5 N). Cupric chloride (2 M aqueous, about 30 mL) was added and the mixture was again neutralized. The addition of cupric chloride and neutralization were repeated twice. The copper complex (a red-brown precipitate which was never collected) was destroyed by adding ammonium hydroxide until the solution was very basic. The solution was then extracted with ether. The organic extracts were washed with water and dried over anhydrous magnesium sulfate. The solvent was removed at reduced pressure and the product distilled bulb-to-bulb at room temperature under oil-pump vacuum to give 0.43 g (50% yield) of the fused azo compound, **2**. NMR ($CDCl_3$): δ 0.85 (m, 2 H, CH_2), 1.18 (s, 3 H, CH_3), 1.61 (s, 3 H, CH_3), 1.7–2.8 (m, 2 H, allylic), 4.85–5.75 (m, 2 H, olefinic + CHN).

Kinetics. A sample of 18–25 mg of the diazene was made up to 1.00 mL total volume in the appropriate solvent, divided into seven 7 × 30 mm Pyrex tubes, and sealed under vacuum. The mineral oil thermostat was kept at the reported temperature ± 0.01 °C over time with a Bayley proportional controller, Model 124. The temperature was measured with a Hewlett-Packard 2801A quartz thermometer calibrated to the freezing point of water. Temperature gradients in the sample region were <0.01 °C.

Samples were removed from the bath from time to time, plunged into liquid nitrogen, allowed to warm to room temperature, centrifuged, and opened. Each tube was analyzed twice, using 50-μL aliquots. The reaction was followed to about 3 half-lives. The correlation coefficients for the fit to a first-order plot were >0.998 in most instances.

The molecular sieves column used for these analyses was made by grinding Linde 13X (10-Å pore size) sieves with mortar and pestle and sieving them to 40/60 mesh. This material was then packed into a $^1/_4$ in. by 6 ft aluminum column. The retention time of nitrogen on this column at 50 °C with 20 psig helium flow was about 4 min. When a considerable amount of organic material (~0.5 mL) had been injected, the retention time decreased noticeably (to about 3 min). When the retention time approached 2 min, the column was regenerated by heating with 20 psig carrier flow to 250–300 °C for several hours, removing the deposited organic material. This was necessary after about every other kinetic run (1.4 mL of solvent having been injected). The injector port of the chromatograph was kept at 230 °C and the detector at 200 °C.

Table II. Kinetics of Thermal Deazetation of Diazene 1 in CH_3CN Solution at 60.63 °C

	N_2 peak area[a]	
time, s	obsd[b]	calcd[c]
0.00	198	212.6
1800	160.5	154.6
3700	113	110.5
5400	86	81.8
5400[d]	87	81.8
8700	45	45.7
12200	24	24.6

$k = 1.77 \times 10^{-4}$ s^{-1}; rms error = 6.7; r = 0.9984

[a] N_2 liberated by pyrolysis of residual 1 in GC injector port. [b] By GC peak area. [c] From slope and intercept of least-squares regression line. [d] Tube packed with glass wool.

Table III. Temperature Dependence of the Rate Constant for Deazetation

	$k \times 10^5$s		
temp, °C	1 in CH_3CN	1 in PhH	2 in CH_3CN
39.97	1.06		
40.01		2.81	2.25
49.98	4.33		
50.00		10.8	7.53
60.50	18.5		36.8 ± 2[a]
60.63	17.9 ± 0.1[a]	42.1	
70.00		137	
70.03	58.8		
70.05			108
80.00			340 ± 15[b]
80.03	206		
E_a, kcal/mol	28.8	27.6	28.0
log A, A in s	15.1	14.7	14.9
$\Delta S^{\ddagger}$, gibbs/mol	8.3	6.5	7.4

[a] Average ± standard deviation of three runs. [b] Average ± standard deviation of two runs.

Table IV. Thermal Rearrangements of the Diazenes **1** and **2** at 50.0 °C in CH_3CN Solution

	1/2 ratio	
time, s × 10^{-3}	from 1	from 2
0	>20	12.8
5.4	15.7	11.4
7.2	12.8	
9.0	7.5	11.0
12.6	6.6	9.6
16.2	5.5	8.2
18.0	4.9	
19.8	4.5	
23.4	3.6	
27.0	2.8	
30.6	2.5	

The nitrogen peak areas were measured with a Hewlett-Packard 3700A digital integrator. Table II presents a sample of the data for a single run. We thank Professor K. B. Wiberg for the use of his computer program for processing the data. Table III shows the temperature dependence and the derived activation parameters.

Kinetics of the 1 → 2 Thermal Rearrangement. Sample tubes containing about 40 mg of **1** or **2** in 350 mL of CH_3CN were prepared and pyrolyzed at 50.0 °C as described for the study of the deazetation kinetics. The tubes were opened and the contents analyzed for the relative amounts of **1** and **2** by evaporation of the solvent, dissolution of the residue in pentane, and filtration through a column of Florisil. The hydrocarbon dimers eluted with pentane, and the diazenes were recovered by elution with ether. Evaporation of the ether (<25 °C) and dissolution of the residue in $CDCl_3$ gave a sample which was treated with enough $Eu(fod)_3$ to cause NMR chemical shift separation of the methyl resonances of **1** and **2**.

Without $Eu(fod)_3$, the methyl groups of the bridged diazene **1** could be detected at δ 1.62, the same chemical shift as one of the two nonequivalent methyl resonances of the fused diazene **2**. The other methyl

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[31] (a) This experiment by Dr. D. M. McDaniel,[31b] to whom we are indebted. (b) Berson, J. A.; McDaniel, D. M.; Corwin, L. R.; Davis, J. H. *J. Am. Chem. Soc.* **1972**, *94*, 5508.

group of **2** appeared at δ 1.20. Addition of Eu(fod)$_3$ caused the downfield resonance at δ 1.62 to separate; the resonance that moved more rapidly downfield depended on the composition of the diazene mixture and the amount of shift reagent added. Identification of **1** and **2** was achieved by comparison of the spectra with those of known Eu(fod)$_3$-treated mixtures.

Control experiments showed that the isolation procedures caused no change in the composition of a known **1**/**2** mixture.

Quantitative analysis of the **1**/**2** ratio was achieved by integration of the bridged methyl peak and the downfield fused methyl peak. The average of 50 integrations was taken for each sample. Table IV gives the results.

Test for Rearrangement in the Photolysis of Bridged Diazene 1. A similar set of samples of 1 in CH$_3$CN solution was irradiated at 0 °C for various extents of deazetation (5–95% conversion) in a Rayonet reactor. The diazene recovered from each sample was analyzed by the above technique and found to contain no fused diazene **2**.

Kinetic analysis of the rearrangement and deazetation was aided by the use of an interactive computer program, kindly provided by Professor Martin Saunders and modified for use with the PDP-1145 computer by Dr. B. K. Carpenter, to whom we are indebted. A subroutine of the differential rate equations corresponding to the triangular scheme of Eq 1 was written, and the program was given trial rate constants and initial concentrations as input data. The program used a Runge–Kutta scheme to integrate the differential equations. Graphs of the fit of the experimental points to the calculated curves are shown elsewhere.[9b]

Product Distribution Studies. The data of Figure 1 were obtained by techniques similar to those described elsewhere.[8]

Acknowledgment. We thank the National Science Foundation (CHE 76-00416) and the National Institute of General Medical Sciences (GM-23375) for grants in support of this work.

Mechanistic Aspects of the Electrochemical Oxidation of Dihydronicotinamide Adenine Dinucleotide (NADH)

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Abstract: The apparently single stage anodic oxidation of NADH involving removal of two electrons and a proton to form NAD$^+$ has been examined with particular attention to the deprotonation step and its relationship to the initial potential-determining electron-transfer step, primarily at glassy carbon electrodes (GCE) in aqueous media with supplementary studies at pyrolytic graphite and platinum electrodes in aqueous media and at GCE in Me$_2$SO; the carbon electrodes were generally first covered with an adsorbed NAD$^+$ layer in order to eliminate adsorption-controlled faradaic processes. The initial step is an irreversible heterogeneous electron transfer (transfer coefficient $\beta = 0.37$ at carbon electrodes and 0.43 at platinum). The resulting cation radical NAD·H$^+$ loses a proton (first-order reaction; rate constant k) to form the neutral radical NAD· which may participate in a second heterogeneous electron transfer (ECE mechanism) or in a homogeneous electron transfer with NAD·H$^+$ (disproportionation mechanism DISP 1 or half-regeneration mechanism), yielding NAD$^+$. The near identities of current functions, viscosity-corrected diffusion coefficients D and β values, point to essentially similar solute species and charge-transfer paths being involved in different media and at different electrodes. D is ca. 2×10^{-6} cm^2 s^{-1} in aqueous solution; k is ca. 60 s^{-1} at the GCE covered with adsorbed NAD$^+$.

The grossly reversible redox behavior exhibited by the NAD$^+$/NADH couple under physiological conditions

$$\mathrm{NAD^+ + H^+ + 2e^- \rightleftharpoons NADH} \qquad (1)$$

has prompted extensive electrochemical study of the reaction. Although polarographic or voltammetric reduction of nicotinamide adenine dinucleotide (NAD$^+$, DPN$^+$, coenzyme I) has been extensively investigated, there are only a few systematic studies of the voltammetric oxidation of 1,4-dihydronicotinamide adenine dinucleotide (NADH).[1-4]

Currently, there is increasing interest in the electrochemical oxidation of NADH (cf. ref 5 and 6 for summaries of recent studies) from the viewpoints of (a) analysis, e.g., in determining compounds which react under enzymatic conditions with NAD$^+$ to produce NADH, (b) using electrochemical approaches and methodology to study biological systems and phenomena, e.g., importance of the NAD$^+$/NADH couple in the electron-transport chain, and (c) using one direction of the NAD$^+$/NADH couple as an electrochemical regeneration step in cyclic redox processes involving chemical transformation and/or energy conversion.

In both aqueous and nonaqueous media, NADH shows a single diffusion-controlled cyclic voltammetric anodic peak; scan reversal produces a cathodic peak due to NAD$^+$. A cathodic peak complementary to the anodic peak, as expected for a reversible redox couple, was not seen at the highest scan rates used (50 V s^{-1} in aqueous media, 10 V s^{-1} in nonaqueous media).

Since mercury is oxidized at the positive potentials at which NADH gives its anodic signal, electrodes of materials such as carbon or platinum must be used. The generally easier oxidation of NADH at carbon (commonly, pyrolytic graphite or glassy carbon) than at platinum electrodes is of general interest because the pronounced increase in background current at both carbon and platinum electrodes makes it difficult to obtain a well-defined limiting current, especially at low NADH concentrations. The increase in background current at platinum starting at 0.5 V can be explained by surface oxide formation; the cause for the background current increase at carbon starting at 0.6 V is uncertain.

Although there has often been a failure to oxidize NADH cleanly at solid electrodes, it is well established that it undergoes a two-electron (2e) oxidation to yield the corresponding enzymatically active nicotinamide (NAD$^+$).[6-9] However, there is still

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(1) A. L. Underwood and R. W. Burnett in "Electroanalytical Chemistry", Vol. 6, A. J. Bard, Ed., Marcel Dekker, New York, 1972, Chapter 1.

(2) P. J. Elving, C. O. Schmakel, and K. S. V. Santhanam, *CRC Crit. Rev. Anal. Chem.*, **6**, 1 (1976).

(3) P. J. Elving, *Top. Bioelectrochem. Bioenerg.*, **1**, 276 (1976).

(4) G. Dryhurst, "Electrochemistry of Biological Molecules", Academic Press, New York, 1977.

(5) J. Moiroux and P. J. Elving, *Anal. Chem.*, **50**, 1096 (1978).

(6) R. D. Braun, K. S. V. Santhanam, and P. J. Elving, *J. Am. Chem. Soc.*, **97**, 2591 (1975).

(7) W. J. Blaedel and R. A. Jenkins, *Anal. Chem.*, **47**, 1337 (1975).

(8) P. Leduc and D. Thevenot, *Bioelectrochem. Bioenerg.*, **1**, 96 (1974); P. Leduc and D. Thevenot, *J. Electroanal. Chem.*, **47**, 543 (1973).

0002-7863/80/1502-6533$01.00/0