Irradiation of **3** in pentane gave tricyclooctane **1** in 70% yield, and no other volatile products. We have not been able to convert **3** to **1** thermally under a variety of conditions. The former observation, taken with others which will be published in the complete paper, suggests that *trans,trans*-1,5-cyclooctadiene may be an intermediate in the copper-catalyzed photochemical conversion of *cis,cis*-1,5-cylooctadiene to tricyclooctane (**1**).

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(14) National Science Foundation Predoctoral Fellow, 1964–1966; National Institutes of Health Predoctoral Fellow, 1966–1967.

(15) Deceased June 4, 1966.

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Spectroscopic Models Related to Coenzymes and Base Pairs.[1] I. The Basis for Hypochromism in the Ultraviolet Spectra of Model Systems Related to Nicotinamide–Adenine Dinucleotide

Sir:

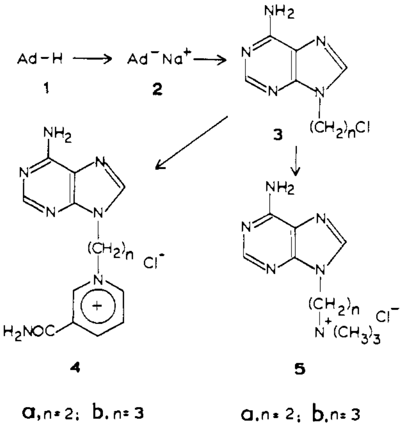
Spectroscopic models have been designed which incorporate aromatic and electrostatic features present in NAD$^+$,[2] *e.g.*, compounds **4** and **5**.[3] Ultraviolet spectroscopic data for **4** should reflect *both* oscillator interaction between the adenyl and the pyridinium rings *and* the possible electrostatic field effect of quaternary nitrogen, whereas the data for **5** should reflect *only* the perturbation of the adenyl chromophore by the positive charge.

Evidence for interaction between the adenyl and pyridinium moieties of NAD$^+$ was obtained by Siegel, *et al.*,[4] who observed decreased adsorbance (8.7%) at the 259-mμ absorption maximum of the intact coenzyme relative to the sum of the absorbancies of the component nucleotides obtained by enzymic hydrolysis. Similar hypochromicity[5] studies were conducted on some NAD$^+$ analogs containing modified adenyl moieties,[6] with the conclusion that the optical anomalies could only be explained by interaction between the component heterocyclic systems.

Although many analogs of the adenine and nicotinamide rings have been incorporated into NAD$^+$ models, and, thus, much attention has been focused on the aromatic moieties involved in the intramolecular interaction, *little attention has been given to models which reflect the possible electrostatic contribution.*

The electrostatic field can be an important factor in a system in which a charge is intimately associated with the chromophore.[8] Moreover, on theoretical grounds it has been demonstrated that hypochromism is a consequence of the effect of the local internal field.[9]

In order to prepare the model compounds Ad-C$_n$-Nic$^+$ (**4**) and Ad-C$_n$-N$^+$ (**5**)[10] designed for ultraviolet study, sodium adenide (**2**)[11] was prepared in DMF from adenine (**1**) and sodium hydride and was alkylated *in situ* with the relevant 1-bromo-*n*-chloroalkane to give the intermediate **3**: **a**, 9-(2-chloroethyl)adenine, mp 206–208°; **b**, 9-(3-chloropropyl)adenine, mp 189–190°. Treatment of **3** with excess nicotinamide in a melt and with excess trimethylamine in tetramethylene sulfone[12] afforded the respective products: **4a**, Ad-C$_2$-Nic$^+$, mp 292–293°; **4b**, Ad-C$_3$-Nic$^+$, mp 255–256°; **5a**, Ad-C$_2$-N$^+$, mp 274–276°; **5b**, Ad-C$_3$-N$^+$, mp 266–268°.



The percentage hypochromism, % $H(\nu)$, for a pair of interacting bases A and B is defined as $[1 - f_{AB}/(f_A + f_B)]100$, where f_{AB} is the oscillator strength of the intact molecule and f_A and f_B are oscillator strengths of the components of the molecule. For example, in calculating the hypochromism of Ad-C$_3$-Nic$^+$, $f_A + f_B$ is the sum of the oscillator strengths of Ad-C$_3$ and Nic$^+$-C$_3$.[3] The ultraviolet absorption curves for NAD$^+$ and the coenzyme models[13] were digitized from the absorption minimum of the 260-mμ (38,460 cm^{-1}) band to the upper wavelength extremity of the band and were compared in absorption intensities with those of the appropriate half-models using the same integration cut-offs.[14]

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(2) This paper is taken in part from the Ph.D. Thesis of P. C. Huang, University of Illinois, 1966.

(3) The following abbreviations are used: Ad-C$_n$-Nic$^+$ for 1-[*n*-(aden-9-yl)alkyl]-3-carbamoylpyridinium chloride; Ad-C$_n$-N$^+$ for *n*-(aden-9-yl)alkyltrimethylammonium chloride; Ad-C$_3$ for 9-propyladenine, mp 178–179°; Nic$^+$-C$_3$ for 1-propyl-3-carbamoylpyridinium chloride, mp 199–200°.

(4) J. M. Siegel, G. A. Montgomery, and R. M. Bock, *Arch. Biochem. Biophys.*, 82, 288 (1959).

(5) The term hypochromicity is used to refer to a decrease in the absorbancy at the absorption maximum of an intact molecule relative to the sum of the absorbancies of the constituent chromophores at selected absorption maxima. Hypochromism, on the other hand, corresponds to an integrated hypochromic effect and is based upon the respective total absorption intensities rather than the absorbancies at the absorption maxima.[7]

(6) (a) G. Pfleiderer, C. Woenckhaus, K. Scholz, and H. Feller, *Ann. Chem.*, **675**, 205 (1964); (b) C. Woenckhaus, *Chem. Ber.*, **97**, 2439 (1964).

(7) M. M. Warshaw and I. Tinoco, Jr., *J. Mol. Biol.*, **20**, 29 (1966).

(8) (a) E. M. Kosower and D. C. Remy, *Tetrahedron*, **5**, 281 (1959); (b) V. Georgian, *Chem. Ind.* (London), 930 (1954); 1480 (1957); C. A. Grob, A. Kaiser, and E. Renk, *ibid.*, 598 (1957).

(9) R. K. Bullough, *J. Chem. Phys.*, **43**, 1927 (1965).

(10) Satisfactory analyses and spectral characterizations were obtained for all new compounds reported.

(11) N. J. Leonard, K. L. Carraway, and J. P. Helgeson, *J. Heterocyclic Chem.*, 2, 291 (1965).

(12) C. K. Bradsher and J. C. Parham, *J. Org. Chem.*, **28**, 83 (1963).

(13) The absorption maxima were very similar for the various models [compound (in H$_2$O), $\lambda_{\max}^{\text{pH } 7.0}$ (mμ), $\lambda_{\max}^{\text{pH } 1.0}$ (mμ)]: NAD$^+$, 258.5, 258; Ad-C$_2$-Nic$^+$, 261, 258.5; Ad-C$_3$-Nic$^+$, 261.5, 259.5; Ad-C$_2$-N$^+$, 260, 257; Ad-C$_3$-N$^+$, 260.5, 258; Ad-C$_3$, 261, 259.5; Nic$^+$-C$_3$, 264, 264; NMN, 265.5, 265.

(14) Digitizing was accomplished using a Benson-Lehner Corp. decimal converter Model F instrument. Numerical integration using Simpson's rule was then carried out using an IBM 7094 computer. We

Hypochromism values are more meaningful than those obtained by considering only the effect at the absorption maxima (hypochromicity), since the phenomenon is actually a function of the relative oscillator strengths.

It was determined by difference spectra that no new absorption band was present in Ad-C_n-Nic$^+$ and that there was no appreciable shift in absorption maximum in comparison with Ad-C_3 + Nic$^+$-C_3.[13] The spectra were run in sufficiently dilute solution to obviate intermolecular interactions.

From the results in Table I it will be seen that the hypochromism value for NAD$^+$ is in the same range as the hypochromicity value[4,5] previously ascribed to the coenzyme. At pH 7.0 the hypochromism of Ad-C_2-Nic$^+$ (7.6%), for which the dihedral angle formed by the planes of the heterocycles can be about 39° at the lower limit, is less than that of Ad-C_3-Nic$^+$ (11.4%), in which the extra methylene link provides greater flexibility and permits limiting folded conformations in which the planes of the heterocycles can be parallel. At pH 1, both rings are protonated and the two positively charged rings should repel each other, rendering unfavorable those conformations which are folded. The negligible hypochromism of Ad-C_3-Nic$^+$ at pH 1.0 results from conformations in which the rings are extended in acid media. The contribution of the positive charge in proximity to adenine can be assessed from the hypochromism values obtained for the models Ad-C_2-N$^+$ and Ad-C_3-N$^+$. The diminution in absorption stemming from the presence of the quaternary ammonium ion in the Ad-C_2-N$^+$ system (12.7%) is even greater than that relating to the nicotinamide ring in the analogous coenzyme model, Ad-C_2-Nic$^+$, which contains both heterocycles. The negligible hypochromism of Ad-C_3-N$^+$ relative to that of Ad-C_2-N$^+$ indicates that the effect of the positive charge alone falls off sharply with distance. By contrast, Ad-C_3-Nic$^+$, in which plane-parallel conformations make maximal oscillator interaction possible and bring the positive charge close to the adenine, exhibits ~11% greater absolute hypochromism than its trimethylammonium counterpart.[15]

Table I. Per Cent Hypochromisms, % $H(\nu)$, of NAD$^+$ and Coenzyme Models at the 260-mμ Band

pH (H_2O)	NAD$^+$	Ad-C_2-Nic$^+$	Ad-C_3-Nic$^+$	Ad-C_2-N$^+$	Ad-C_3-N$^+$
7.0	9.0	7.6	11.4	12.7	0.1
1.0	5.5	−2.9	−0.8	1.1	−0.6

Complete assessment of the relative importance of oscillator interaction between adenine and nicotinamide and of perturbation by the positive charge on nicotinamide is not possible, partly because the charge delocalization in the pyridinium system leaves only fractional positive charge on nitrogen and partly because the relative populations of similar conformations of Ad-C_n-Nic$^+$ and Ad-C_n-N$^+$ may not be directly comparable. What can be concluded from this study, however, is that, for NAD$^+$-type systems in aqueous solution, the hypochromism observed in their ultraviolet spectra will be a function of both (a) conformation favorable for interaction between the N-substituted nicotinamide and the adenine and (b) proximity of the positive charge to the adenine ring system. In sequels, additional studies on the ultraviolet and fluorescence spectra of spectroscopic models related to coenzymes and dinucleotide base pairs will be reported.

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wish to express our appreciation for the generous assistance of Professor J. Jonas.

(15) F. Hirayama, *J. Chem. Phys.*, **42**, 3163 (1965), has shown in a different kind of experiment with an analogous homocyclic aromatic model, Ph$(CH_2)_n$Ph, that aromatic interaction was uniquely favored when $n = 3$.

A Remarkably Stable Simple Thiepin

Sir:

Although thiepin and simple monoannulated derivatives of thiepin have not been described,[1] highly substituted thiepins which contain a cyclic eight-π-electron system have been prepared.[2] Generally these heterocycles undergo thermal rearrangement with loss of sulfur, their instability sharply increasing with decreasing ring substitution. Indeed, one attempt to synthesize an unsubstituted benzothiepin resulted only in the formation of sulfur-free products.[3] In marked contrast to these observations, we wish to report that thieno[3,4-*d*]thiepin (I), an unsubstituted monoannulated thiepin system, exhibits remarkable thermal stability.

Periodate oxidation[4] of 4,5-dihydrothieno[3,4-*d*]thiepin (II)[5] in aqueous methanol gave in 97% yield the corresponding vinyl sulfoxide III, mp 78°.[6] Brief treatment of III with freshly distilled acetic anhydride at 150° in the absence of oxygen followed by thick layer chromatography of the reaction mixture resulted in the isolation of bright yellow crystals of I, mp 149–151°, in 50% yield.[7]

The thiepin structure for I was indicated by its mass spectrum which showed a major fragment at *m/e* 134, the ion of benzo[*c*]thiophene (IV),[8] as well as the parent ion at 166.[9] Additionally, the nmr spectrum of I in $CDCl_3$ exhibits singlet resonance at δ 6.64 (two protons) and a quartet of bands centered at δ 6.06 and 5.22 (four protons), which is in accord with the assigned structure. Absorption maxima at $\lambda_{\max}^{\mathrm{MeOH}}$ 210 mμ (log ε 4.13), 224 (4.12), 228 (4.15), 245 (4.29), 1251 (4.41), 260 (4.41), 308 (3.23), 318 (3.30), 331 (3.27), 346 (3.03), 369 (2.56), 378 (2.49), and 390 (2.43) indicate extended conjugation to be present in I.

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(1) R. Zahradnik, *Advan. Heterocyclic Chem.*, 1, (1965).

(2) For examples, see (a) H. Hofmann and H. Westernacker, *Angew. Chem.*, **79**, 238 (1967); (b) M. J. Jorgenson, *J. Org. Chem.*, **27**, 3224 (1962); (c) J. D. Loudon and A. D. B. Sloan, *J. Chem. Soc.*, 3262 (1962); (d) V. J. Traynelis and R. F. Love, *J. Org. Chem.*, **26**, 2728 (1961).

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(8) R. Meyer, H. Kleinert, S. Richter, and K. Gewald, *J. Prakt. Chem.*, **20**, 244 (1963).

(9) Mass spectra were obtained at 70 ev. Peaks at *m/e* 166 and 134 showed correct ^{34}S isotopic abundance.