The α-helical forms of PHEG and PGA display similar CD spectra,[8] as shown in Figures 2 and 3. Dilute salt has little effect upon the CD of PGA at pH 4.4. Helix formation is complete at this pH.[9] All three CD peaks of PGA enlarge (by approximately the same amount) as the PGA concentration increases. For example, $[\theta]_{222}$ in water averages $-37{,}600$ for the concentration range 0.01–0.03% PGA, $-40{,}800$ for 0.04–0.08%, and $-43{,}100$ for 0.09–0.20%. Each range includes seven different concentrations, average errors are ± 2000, and readings did not change with time. Somewhat less concentration dependence was noticed in 0.2 *M* salt. The observed effect of PGA concentration upon CD can be attributed to aggregation of helices.[9-12]

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(7) Furthermore, the "random coil" forms undergo additional change upon heating. At pH 7.7 in 0.2 *M* $NaClO_4$, $[\theta]_{198}$ for both PHEG and PGA gradually decreases, reaching the same limiting value of $-16{,}000$ for both polymers at 90°.

(8) The differences between these CD spectra are within experimental error. However, the differences are of the type noted as a helix solvent effect by F. Quadrifoglio and D. W. Urry, *J. Am. Chem. Soc.*, **90**, 2755 (1968).

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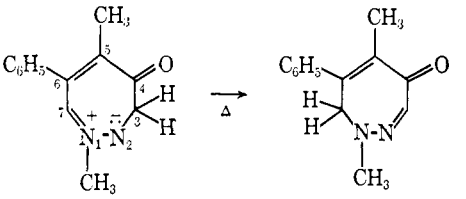
A. J. Adler, R. Hoving, J. Potter, M. Wells, G. D. Fasman
Contribution No. 591, Graduate Department of Biochemistry Brandeis University, Waltham, Massachusetts 02154
Received May 9, 1968

Heterocyclic Studies. XXVIII. Sigmatropic and Electrocyclic Reactions in the 1,2-Diazepine System. Formation of a 1,7-Diazabicyclo[4.1.0]heptenone[1]

Sir:

We wish to report novel examples of a sigmatropic rearrangement and an electrocyclic reaction occurring in a seven-membered heterocyclic ring and isolation from the latter reaction of a [4.1.0] valence isomer of the 1,2-diazepine system. Reactions of this bicyclic product have clarified the mechanism of several rearrangements previously observed in this series.

The 1,2-diazepinium betaine **1**, obtained by methylation of the 2,3-dihydrodiazepinone,[2,3] rearranges on standing in the solid state or in solution to the 1-methyl-1,7-dihydrodiazepinone **2**.[4] We have now found that in $CDCl_3$–CD_3OD solution no significant deuterium exchange occurs on conversion of **1** to **2**; the nmr spectrum of **2** showed signals for C–Me, N–Me, 7-CH_2, and 3-CH in intensity ratio 3.0:3.0:1.9:1.0. The rate constants, determined spectrophotometrically in methanol and chloroform, and kinetic parameters are given in Table I.



1 **2**

The absence of deuterium in the diazepinone **2** obtained in the presence of CD_3OD, the somewhat higher rate in a nonprotic solvent, and the magnitude of the activation energy indicate that the transformation is not a prototropic tautomerization, as previously suggested,[3] but rather a concerted intramolecular process, *i.e.*, a thermally allowed 1,5-sigmatropic hydrogen shift of a type well precedented in the cycloheptatriene series.[5]

Table I. First-Order Rate Constants (k_1)[a] and Activation Parameters for the Thermal Rearrangement **1** → **2**

Solvent	$k_1 \times 10^4$ sec^{-1}, 25.0 ± 0.1°	$k_1 \times 10^4$ sec^{-1}, 35.0 ± 0.1°	E_a, kcal/mol	$\Delta S^{\ddagger}$, eu
CH_3OH	2.4	6.0	+17	−21
$CHCl_3$	3.0	9.0	+20	−9

[a] Plotted by the Guggenheim method.

To examine the possibility of a 1,3-sigmatropic rearrangement in the photoexcited state, a solution of the betaine **1** in methanol–chloroform was exposed to sunlight at −80°. After 35 min, **1** had disappeared and the solution was evaporated to an oil which was chromatographed on silicic acid. The initial fraction contained a trace of the 1,5-dihydrodiazepinone **3**[6] (~2% yield), identified by the nmr spectrum [δ 1.05 (d, J = 7 Hz), 3.70 (s), 6.65 (s)]. The major product (80% yield by nmr of crude mixture, 70% by weight of chromatographic fractions) crystallized as off-white prisms: mp 72–75°; ν_{CO}^{KBr} 1665 cm^{-1}; λ_{max}^{MeOH} 278 mμ (ε 11,000), 342 (shoulder); nmr ($CDCl_3$) δ 1.85 (s, 3), 2.62 (s, 3), 3.20 (s, 1), 3.64, 3.96 (dd, AB J = 18 Hz), 7.43 (s, 5). *Anal.* Calcd for $C_{13}H_{14}ON_2$: C, 72.87; H, 6.59; N, 13.08. Found: C, 73.16; H, 6.67; N, 13.09. The compound could be sublimed to give pale yellow crystals, but exposure of the solid to light caused a deep carmine coloration on the surface due to a photochromic effect.

The spectral properties of this photoisomer clearly reveal the structure as 4,7-dimethyl-5-phenyl-1,7-diazabicyclo[4.1.0]-4-hepten-3-one (**4**), arising by a concerted 4π electrocyclic reaction of the azomethine imine system in **1**. A related photocyclization has recently been postulated in the conversion of a 1-iminopyridinium betaine to 1-ethoxycarbonyl-1,2-diazepine,[7] but the diaziridine was not isolated. The 1,5-dihydrodiazepinone **3** is presumably the product of a competing 4π sigmatropic rearrangement of **1**, but formation of a trace of **3** by thermal rearrangement of **1** to **2** and subsequent photochemical conversion of **2** to **3** cannot be excluded. A third product present in the more polar fractions of the photolysis mixture (~25% by nmr) was the 6-methylaminopyridine **5**.[3] This pyridine

(1) Supported by Grant GP-5219 from the National Science Foundation.

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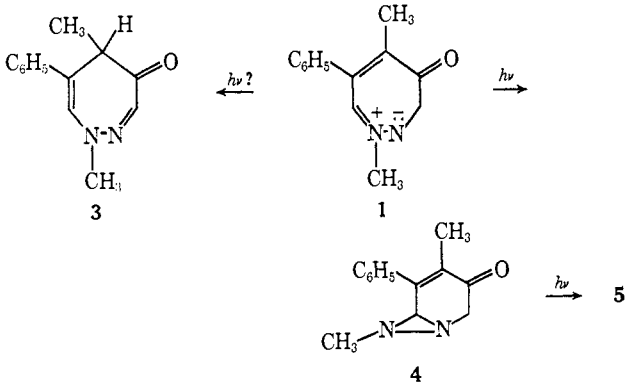
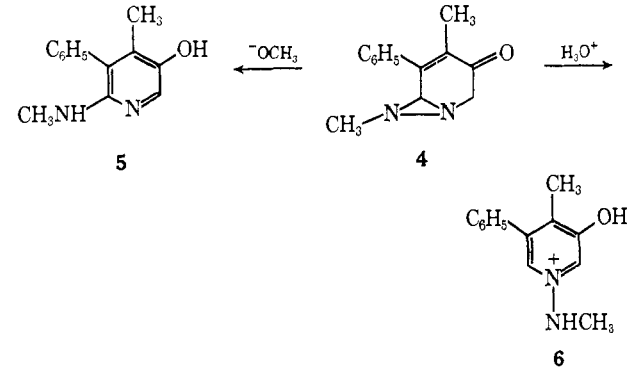
arises by a secondary photochemical reaction of **4** as shown by separate irradiation of the latter.



The bicyclo[4.1.0] ketone **4** is of particular importance in this series since intermediates with this ring system have been postulated in both acid-catalyzed rearrangements of the 2,3-dihydrodiazepinone system to 1-aminopyridines[2] and more recently also in the base-catalyzed rearrangement of the 1,5-dihydro- or 1,7-dihydrodiazepinones to 6-aminopyridines.[4,6] In accord with these suggestions, we have found that **4** is in fact converted very rapidly in methanolic hydrochloric acid into the 1-methylaminopyridinium chloride **6** and in methanolic sodium methoxide into the 6-methylaminopyridine **5**. The nmr spectra of the reaction mixtures in each case indicated a single product; **5** and **6** were isolated and compared (melting point, ir and uv spectra) with samples described previously. These reactions demonstrate that bicyclo[4.1.0] species such as **4** can serve as precursors of both types of pyridine products.



Melvin G. Pleiss, James A. Moore
Department of Chemistry, University of Delaware
Newark, Delaware 19711
Received June 17, 1968

Observation of a Helix–Coil Transition by Pulsed-Field-Gradient Spin–Echo Nuclear Magnetic Resonance

Sir:

Poly-L-glutamic acid has been shown to undergo a helix to random coil conformational change as a function of pH.[1,2] At low pH the helical conformation is the more stable form, and at high pH the random coil is the more stable. The pH at the transition midpoint has been reported to be 5.1 in 1 *M* NaCl,[3] 5.8 in H_2O,[2] and 6.0 in D_2O with 0.2 *M* NaCl.[4] This note describes a study of this conformational change by the study of the translational self-diffusion coefficient by pulsed-field-gradient spin–echo nmr spectroscopy.[5,6]

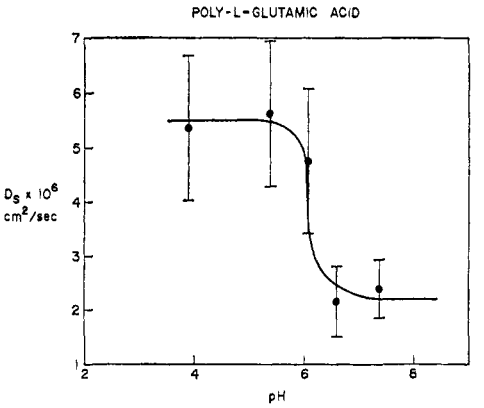


Figure 1. The self-diffusion coefficient, D_s, of poly-L-glutamic acid in D_2O at 25° at various pH values.

The polypeptide solutions were prepared by adding 35.8 mg of Pilot Chemical Co. sodium poly-L-glutamate monohydrate (DP 530) to 1.5 ml of 0.5 *M* phosphate buffer solutions of the desired pH. The sample tubes were then connected to a vacuum system, and the solutions were freeze dried and redissolved in 99.8 mole % D_2O from Stohler Isotope Chemicals. This was repeated three times, and the final time the volumes of the solutions were adjusted to 1.2 ml. The samples were then sealed, still under vacuum. This left only protons in nonexchangeable positions on the poly-L-glutamic acid in the sample, with a very few residual protons in the D_2O.

The self-diffusion coefficient of poly-L-glutamic acid was measured by measuring the self-diffusion coefficient of the protons in the sample by pulsed-field-gradient spin–echo nmr. Figure 1 shows the plot of self-diffusion coefficient D_s at 25° *vs.* the pH of the sample. Each value of D_s is the average obtained from measurements at four values of the magnetic field gradient, and the results of 20 echo amplitude determinations were averaged for each choice of the field gradient. The error limits in Figure 1 indicate the standard deviation of these measurements. The large uncertainties in D_s values result from a roughly ±10% limitation in the determination of the echo amplitudes.

The smaller self-diffusion coefficient at higher pH is compatible with the unfolding of the polypeptide into a bulkier random-coil conformation. It thus appears feasible to study conformational changes in biological systems by the measurement of the self-diffusion coefficient by spin–echo nmr.

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(7) Address inquiries to the Department of Chemistry, University of Indiana, Bloomington, Ind.

Robert E. Moll[7]
Department of Chemistry, Stanford University
Stanford, California
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