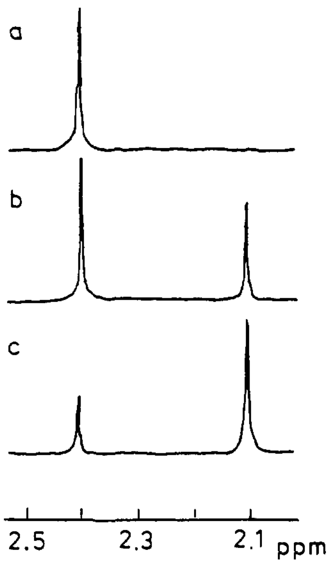

Figure 2. NMR spectra of **1** in cyclohexane-d_{12} and mixed solvents of cyclohexane-d_{12} and ethanol-d_6: (a) in cyclohexane-d_{12}; (b) in a cyclohexane-d_{12}–ethanol-d_6 mixture (volume ratio, 98:2); (c) in a cyclohexane-d_{12}–ethanol-d_6 mixture (volume ratio, 85:15).

the reaction is allowed when the conformation converts to the C_2 symmetry, or antiparallel orientation, as shown in Scheme I.

Parts a and b of Figure 1 show the optical absorption spectra of **1** in cyclohexane and ethanol, respectively, upon irradiation with 313-nm light. The absorption band around 525 nm is due to the closed-ring form.[1a] Although the photocyclization proceeded in ethanol, it was completely prohibited in cyclohexane. This suggests that the conformation of **1** is fastened in parallel orientation in cyclohexane by intramolecular hydrogen bonding. If so, the hydrogen bonding is expected to be broken by ethanol or heating. In fact, the addition of a very small amount of ethanol activated the photoreactivity. In a mixed solvent of cyclohexane and ethanol (volume ratio, 98:2) the quantum yield of photocyclization was 0.29. It further increased with increasing ethanol content and reached a plateau value of 0.51 in the solvent containing 15 vol % ethanol. **1** became photoactive by the addition of not only alcohols but also other hydrogen-bond-breaking agents, such as propylamine. In decalin, the photoreaction occurred at temperatures higher than 100 °C.

In order to confirm the above reaction mechanism, ^{1}H NMR spectra of the molecule were measured in cyclohexane-d_{12} and in mixed solvents of cyclohexane-d_{12} and ethanol-d_6, as shown in Figure 2. The methyl protons at the 2-position of the benzothienyl rings give information concerning the relative population of the two conformations. The protons give signals at different fields depending on the conformation, that is, whether the aryl rings are parallel or antiparallel.[3] The upper field signal is attributed to the protons in the parallel conformation, while the lower field signal points to the antiparallel conformation.

In cyclohexane the upper field signal was not observed, while it appeared upon the addition of ethanol. The ^{1}H NMR spectra clearly indicate that the molecule was in the parallel conformation in cyclohexane. It converted to the antiparallel conformation upon the addition of a small amount of ethanol. The absence of photocyclization in cyclohexane is explained by the clasped parallel conformation. Intramolecular hydrogen bonding fastened the molecule into the parallel conformation and made it photochemically inactive. Conversely, ethanol acted as a switch to unclasp the system. The dimethyl ester derivative of **1** did not show any such solvent dependence.

The contribution of intermolecular hydrogen bonding was considered to be negligible, because any upper field signal was not discerned in cyclohexane. When the carboxyethyl groups were replaced with carboxymethyl groups, compound **2**, a weak 525-nm band appeared even in cyclohexane. This suggests that carboxymethyl groups did not fit to make rigid intramolecular hydrogen bonding, and intermolecular bonding existed to some extent.

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Registry No. 1, 143619-58-3; **1** dimethyl ester, 143619-59-4; **1** closed-ring form, 143619-60-7; **2**, 143619-61-8; ethanol, 64-17-5.

Design at Nanometric Dimensions To Enhance Hydrophobicity-Induced pK_a Shifts

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With poly[4(GVGVP),(GEGVP)] (I) as a reference state, the polytricosapeptides, poly[3(GVGVP),2(GFGFP),(GEGFP)] (II), poly[2(GVGVP),2(GVGFP),(GFGFP),(GEGFP)] (III), poly(GEGFPGVGVPGVGVPGVGVPGFGFPGFGFP) (IV), and poly(GEGFPGVGVPGVGFPGFGFPGVGVPGVGFP) (V), all having the same theoretical and essentially the same analytical amino acid compositions,[1] were synthesized and designed for the specific purpose of testing the limits of hydrophobicity-induced pK_a shifts in this system. Polymers I, II, III, IV, and V exhibited pK_a values for the Glu (E) residues of 4.3, 4.7, 6.3, 7.7, and 8.1, respectively. Due to the limited number of Glu residues, the structures themselves exclude the often invoked charge–charge interaction mechanism for pK_a shifts. The differences in pK_a values arise from the differences in proximity of the Glu (E) and Phe (F) residues within and between pentamers with optimal arranging of five nearest-neighbor Phe residues at nanometer distances from the Glu residue in IV and V. This remarkable increase of 3.8 pH units overall demonstrates a repulsive free energy of interaction between hydration processes of the Phe and Glu side chains of 5 kcal/mol. To our knowledge these are the largest pK_a shifts documented for the Glu residue, and the recently identified interactions responsible are considered to be important free energies of interaction in modulating protein structure and function.[2]

Polymers IV and V were designed on the basis of the working β-spiral structure of poly(GVGVP), shown schematically in Figure 1A.[2,3] For the β-spiral structure, the distance between turns is approximately 1 nm.[4] This results in the nanometer proximities of the Glu and Phe residues shown in Figure 1B. The polytricosapeptides were constructed by the sequential addition of pentamers. The composite pentamers were also mixed in the appropriate ratios and polymerized to obtain polymers II and III without fixed ordering of pentamers. A complete description of the syntheses will be presented elsewhere. The structures were verified by carbon-13 nuclear magnetic resonance and amino acid analyses. The resolved acid–base titration data, for one experiment of three, for each of the five polymers are given in Figure 2, and the standard deviations for three runs each for the polymers were less than ±0.1 pH units.

Polymers of the composition poly[f_V(GVGVP),f_X(GXGVP)], where f_V and f_X are mole fractions with $f_V + f_X = 1$ and where X can be any amino acid residue, undergo phase transitions, the

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(1) The single-letter codes for the amino acid residues are Gly (G), Val (V), Pro (P), Glu (E), Phe (F), and Trp (W).

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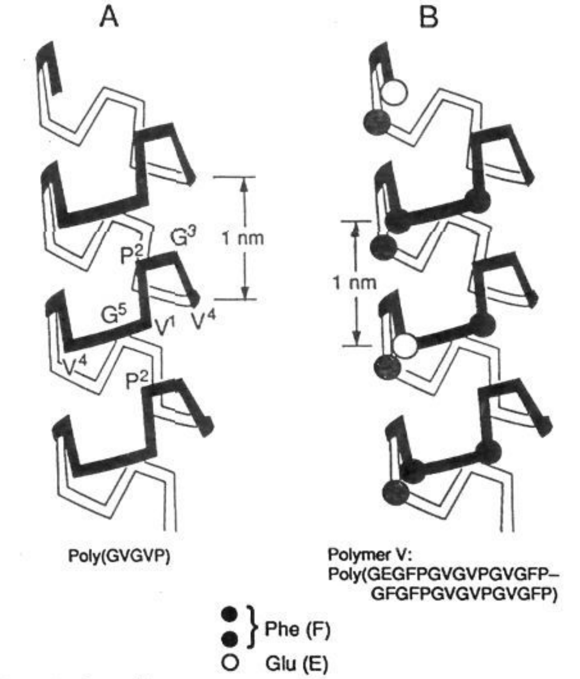

Figure 1. Controlling pK_a by design at nanometric dimensions: Schematic representation of the β-spiral structure proposed for the polypentapeptide poly(Val^1-Pro^2-Gly^3-Val^4-Gly^5), which is equivalent to poly(GVGVP). The Pro^2-Gly^3 β-turn is seen to function as a spacer between the turns of the β-spiral in A, and the hydrophobic folding arises principally from interturn Val^1 γ-CH$_3$ $\leftrightarrow$ Pro^2 β-CH$_2$ interactions. In B, the Phe residues are placed proximal to the Glu residues on the basis of a β-spiral with approximately 3 pentamers per turn, i.e., on the basis of tertiary structure.

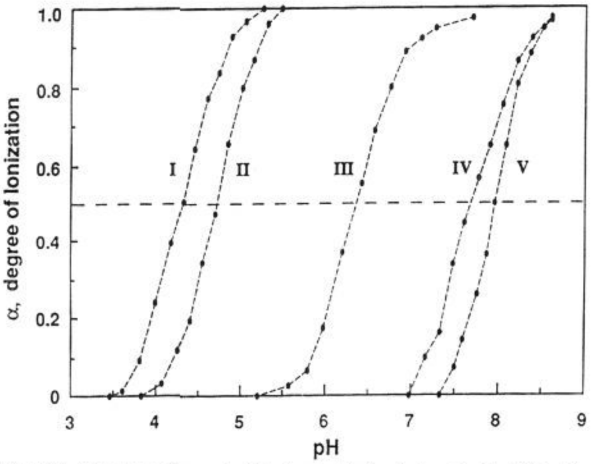

Figure 2. Structure dependent hydrophobicity-induced pK_a shifts: Resolved acid-base titration curves which give pK_a values of 4.3, 4.7, 6.3, 7.7, and 8.1 for polymers I-V, respectively. A remarkable overall pK_a shift of 3.8 pH units is observed. For all curves, the starting concentration was 40 mg/mL and the temperature was 20 °C.

temperatures (T_t) for which vary systematically with composition.[2] Plots of T_t vs f_X are linear, with more hydrophobic residues lowering T_t and less hydrophobic residues increasing T_t. This property has been used to develop a hydrophobicity scale for amino acids.[5] The values of T_t, extrapolated to $f_X = 1$, range from −90 °C for poly(GWGVP) to 250 °C for poly(GEGVP) with Glu-(COO$^-$). The mean residue hydrophobicities, $\langle T_t \rangle$, calculated using this hydrophobicity scale and the amino acid analysis data are 30, 23, 20, 22, and 21 °C for polymers I-V, respectively, in the Glu COOH state, yet the pK_a values differ remarkably.

Previous studies have shown that increased hydrophobicity increases pK_a,[2,6,7] yet in this molecular system tertiary structure dominates over primary structure in achieving the largest pK_a shift. Mean residue hydrophobicity calculations using a sliding window of 11 residues,[5] $\langle T_t \rangle_{11}$, give 15 for polymer IV and 20 for V for the Glu COOH state, and 35 for IV and 40 for V for the Glu COO$^-$ state. Thus, on the basis of primary structures, the Glu residues in polymer IV would experience the greater hydrophobicity and would be expected to give the larger pK_a shift. The pK_a shift is greater, however, for polymer V. Only when the proper, β-spiral folding is taken into account does the spatial proximity become apparent, and this Glu-Phe proximity, as shown in Figure 1B, provides the understanding for the larger pK_a shift exhibited by polymer V.

Clearly, the differences in pK_a do not arise from the commonly considered electrostatic interactions.[8,9] The pK_a shifts instead are an expression of a repulsive free energy of interaction which exists between the hydration shells of hydrophobic and polar (COO$^-$) moieties when sufficiently proximal as discussed in more detail elsewhere.[2] The change in Gibbs free energy per mole obtained from the change in chemical potential, $\Delta\mu$, required to maintain 50% ionization of the side chain is given by $\Delta\mu = -2.3RT\Delta pK_a$. At 20 °C with a ΔpK_a of 3.8 pH units, $\Delta\mu$ is 5.1 kcal/mol; there is observed a repulsive Gibbs free energy of interaction arising out of the proximity of Phe and ionized Glu side chains in polymer V.

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Synthesis, Self-Assembly, and Photophysical Dynamics of Stacked Layers of Porphyrin and Viologen Phosphonates

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Organic thin films are of ongoing interest as photoconductors, photovoltaics, electrochromics, and nonlinear optical elements.[1] Photo- or electroactive species in such films would be best utilized if assembled repetitively in specific sequences or orientations in durable matrices. The self-assembly of transition metal phosphonates on surfaces[2] provides an attractive means of constructing thermally and solvolytically stable films of controlled thickness with spatially defined molecular components. Recently we reported the synthesis, multilayer formation, and nonlinear optical behavior of a polar chromophoric phosphonic acid that self-assembles on Zr phosphate surfaces.[3] Mallouk et al. have incorporated electroactive species into inert phosphonate matrices by ion exchange to form a rectifying film.[4] Film components capable

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