puter. We found that $K_{m,peptide} = (40 \pm 10) \times 10^{-6}$ M, as measured spectrophotometrically, and $(30 \pm 10) \times 10^{-6}$ M, as determined from rate measurements employing adenosine 5'-[γ-^{32}P]triphosphate, while a value of $k_{cat} = 3000 \pm 200$ min^{-1} was obtained in both types of experiments. For analytical purposes, peptide **1** was enzymatically phosphorylated on a preparative scale by a procedure similar to that described elsewhere for Leu-Arg-Arg-Ala-Ser-Leu-Gly.[8] The final phosphorylated product gave an amino acid analysis of Arg (2.0), Gly (1.0), Leu (2.0), Ser (0.88), and (o-NO_2)Tyr (1.0) on acid hydrolysis. The phosphate content was determined to be 1.10 mol/mol of peptide.[9]

In a recent paper we reported that the bovine cardiac muscle protein kinase shows a marked preference for the Mg(II) complex of the A isomer of ATPβS.[7] In order to monitor the transfer of the γ-phosphoryl group to the peptide substrate Leu-Arg-Arg-Ala-Ser-Leu-Gly, it was necessary to prepare each of the diastereomers of ATPβS in a radioactively labeled form (γ-^{32}P label).[10] Now that we have in hand a peptide substrate, **1**, which undergoes a significant spectral change on phosphorylation, it is possible to study the stereochemical preference of protein kinase for metal–nucleotide complexes without having to resort to radioactive labeling of the nucleotide. For example, a brief investigation of the action of protein kinase on the A and B isomers of ATPαS was undertaken by using **1** as the peptide substrate.[11] Under conditions identical with those given above for the reaction with ATP, with **1** at a concentration of 100 μM, and ATPαS B at a concentration of 2 mM, the phosphorylation reaction proceeded to completion at 13% of the rate observed at [ATP] = 2 mM. When ATPαS A isomer (2 mM) was employed, however, only 15% of the peptide appeared to be phosphorylated and the rate of the reaction observed was 3% of that seen for ATP under comparable conditions. We believe that this result is due to contamination of ATPαS A with a very small amount ($\sim$0.75%) of another nucleotide, possible ATP. Indeed, when an amount of ATP corresponding to the putative contaminant was added to the solution of ATPαS A, phosphorylation of 30% of the peptide was observed to occur, proceeding at a rate which was 4% of that seen with 2 mM ATP. In line with these experiments, when the concentration of ATPαS A was reduced to 50 μM, no phosphorylation of the peptide was detected spectrophotometrically. At a concentration of 50 μM, the ATPαS B isomer reacted at a rate at least 300 times greater than the minimum we would have detected. Thus, our results demonstrate that protein kinase has a definite preference for the Mg(II) complex of the B isomer of ATPαS. While the Mg(II) ion presumably is coordinated to the β,γ-positions of the triphosphate moiety of ATP when the metal–nucleotide complex is bound to the enzyme, our findings may indicate that coordination of the metal ion to the α position is important in the transition state for γ-phosphoryl transfer reactions catalyzed by protein kinase, but additional studies with other metal ions will be needed to test this possibility. Further studies on the metal ion dependence and stereochemical preferences of the catalytic subunit of the bovine cardiac muscle enzyme are currently under way with peptide **1** as the substrate.

Acknowledgment. We thank Professor F. Eckstein for a generous gift of ATPαS A and B isomers, and Professor R. Heinrikson and Ms. P. Keim for the amino acid analyses. This research was supported by Grant GM 19037 from the National Institutes of Health and Grant CA 17150 from the National Cancer Institute, DHEW.

(8) Granot, J.; Mildvan, A. S.; Hiyama, K.; Kondo, H.; Kaiser, E. T. *J. Biol. Chem.*, **1980**, *255*, 4569.
(9) Ames, B. N. *Methods Enzymol.* **1966**, *8*, 115.
(10) Stingelin, J.; Bolen, D. W.; Kaiser, E. T. *J. Biol. Chem.* **1980**, *255*, 2022.
(11) Eckstein, F. *Acc. Chem. Res.* **1979**, *12*, 204.

H. Neal Bramson, Nancy Thomas, William F. DeGrado
E. T. Kaiser*
Department of Chemistry, The University of Chicago
Chicago, Illinois 60637
Received May 5, 1980

Biomimetic 8α Functionalization of Riboflavin

Sir:

Over the last 20 years flavins bound covalently to flavoenzymes[1] have been isolated from sources ranging from mammalian brain tissue to soil bacteria. Generally, the linkage is through the 8α-methyl group of the isoalloxazine nucleus (**1**) to an imidazole nitrogen of histidine[2] or sulfur of cysteine.[3] A recent hypothesis forwarded by Walsh[4] predicts the genesis of the 8α-peptidyl flavins via the quinone methide tautomer (see **2**) of riboflavin (see tetraisobutyryl derivative **1**, Scheme I). Herein we report model studies which establish chemical precedent for facile tautomerization of flavins and interception of the resulting quinone methide, **2**, by nucleophiles.

During the course of our investigations of flavin monooxygenase activity,[5] we discovered that certain cyclic tertiary amine N-oxides, **6a–c** (Table I), catalyze the conversion of tetraisobutyrylriboflavin (**1**) into a brilliant red, crystalline dimer, **4a**[6] (field-desorption MS, M^+ m/e 1311). This conversion is also effected by the tertiary amine base 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU, **7**). Potassium phenolates **8a,b** (Table I) convert **1** into a mixture of tautomeric red and orange dimers, **4a** and **5a**,[7,8] respectively. Dimer **4a** upon hydrolysis of the isobutyryl esters is converted into **4b**, previously reported by Hemmerich.[9a,10] In contrast to the

(1) Reviews: (a) "Flavins and Flavoproteins, Proceedings of the Fifth International Symposium"; Singer, T. P., Ed.; Elsevier: New York, 1976; pp 271–381. (b) Berezovskii, V. M.; Zhilina, T. A. *Chem. Nat. Prod.* **1979**, 219. (c) "Flavins and Flavoproteins, Proceedings of the Sixth International Symposium"; Yagi, K., Yamano, T., Eds.; University Park Press: Baltimore, 1980; pp 237–289.

(2) (a) Walker, W. H.; Singer, T. P.; Ghisla, S.; Hemmerich, P. *Eur. J. Biochem.* **1972**, *26*, 279. (b) Mohler, H.; Brühmüller, M.; Decker, K. *Ibid.* **1972**, *29*, 152. (c) Pinto, J. T.; Frisell, W. R. *Arch. Biochem. Biophys.* **1975**, *169*, 483. (d) Kenney, W. C.; Edmondson, D. E.; Seng, R. L. *J. Biol. Chem.* **1976**, *251*, 5386. (e) Kenney, W. C.; Edmondson, D. E.; Singer, T. P.; Steenkamp, D. J.; Schabort, J. C. *Biochemistry* **1976**, *15*, 4931. (f) Ghisla, S.; Hartmann, U.; Hemmerich, P. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 642. (g) Edmondson, D. E.; Kenney, W. C.; Singer, T. P. *Biochemistry* **1976**, *15*, 2937.

(3) (a) Walker, W. H.; Kearney, E. B.; Seng, R. L.; Singer, T. P. *Eur. J. Biochem.* **1971**, *24*, 328. (b) Walker, W. H.; Kenney, W. C.; Edmondson, D. E.; Singer, T. P.; Cronin, J. R.; Hendriks, R. *Ibid.* **1974**, *48*, 439. (c) Kenney, W. C.; Singer, T. P. *J. Biol. Chem.* **1977**, *252*, 4767. (d) Ghisla, S.; Hemmerich, P. *FEBS Lett.* **1971**, *16*, 229.

(4) Walsh, C. T. *Acc. Chem. Res.* **1980**, *13*, 148.

(5) (a) Rastetter, W. H.; Gadek, T. R.; Tane, J. P.; Frost, J. W. *J. Am. Chem. Soc.* **1979**, *101*, 2228. (b) Rastetter, W. H.; Frost, J. W. *Tetrahedron Lett.* **1979**, 3353.

(6) Data for **4a**: ^{1}H NMR (60 MHz, dimethyl-d_6 sulfoxide) (Me_4Si) δ 0.6–1.2 (m, 48 H), 1.9–2.9 (m, 8 H, partially obscured by solvent), 2.7 (s, 6 H), 3.3 (s, exchangeable H plus H_2O), 4.0–5.6 (br m, 14 H), 7.9 (s, 2 H), 8.1 (s, 2 H), 8.3 (s, 2 H), 11.6 (s, 2 H); ^{13}C NMR (15 MHz, dimethyl-d_6 sulfoxide) (Me_4Si) δ 174.9–175.5 (multiple lines), 170.1, 159.5, 155.0, 150.8, 142.4, 137.7, 135.1, 134.8, 131.4, 112.7 (low intensity, two lines?), 69.4 (multiple lines), 61.6 (multiple lines), 33.2 (multiple lines), 18.4 (multiple lines); IR (KBr) 2980, 1740, 1575, 1535, 1470, 1400, 1350, 1250, 1185, 1150, 830, 810, 750, 680, 475 cm^{-1}; UV (HCOOH) λ_{max} 500 (ϵ 6.0 $\times$ 10^4), 484 shoulder (ϵ 5.6 $\times$ 10^4), 262 (ϵ 6.4 $\times$ 10^4), 280 nm shoulder (ϵ 3.6 $\times$ 10^4). Anal. Calcd for $C_{66}H_{86}N_8O_{20}$: C, 60.43; H, 6.62; N, 8.54. Found: C, 60.51; H, 6.49; N, 8.33. Field-desorption MS, see text.

(7) Data for **5a**: (a) ^{1}H NMR (90 MHz, $CDCl_3$) (Me_4Si) δ 0.8–1.2 (m, 48 H), 2.5 (s, 6 H), 2.2–2.8 (m, 8 H), 3.3 (s, 4 H), 4.5–5.6 (br m, 14 H), 7.7 (s, 2 H), 8.1 (s, 2 H), 8.9 (s, 2 H); ^{13}C NMR (62.9 MHz, $CDCl_3$) (Me_4Si) δ 176.0–176.6 (multiple lines), 159.3, 154.7, 150.7, 150.0 (2 lines), 136.5, 134.5, 133.8, 131.2, 114.8, 70.4, 69.0 (two lines), 61.8, 44.5, 33.7–34.1 (multiple lines), 18.3–19.0 (multiple lines); IR (KBr) 2980, 1740, 1700, 1580, 1540, 1460, 1380, 1340, 1240, 1180, 1140 cm^{-1}; UV (HCOOH) λ_{max} 444 (ϵ 6.7 $\times$ 10^3), 372 (ϵ 5.5 $\times$ 10^3), 252 (ϵ 2.8 $\times$ 10^4), 274 nm shoulder (ϵ 1.8 $\times$ 10^4). Field-desorption MS, M^+ m/e 1311. (b) The structural assignment for dimer **5a** is based on the measured parent ion m/e and the similarity of the ^{1}H, ^{13}C NMR, and UV spectra with those measured for flavin **1**: ^{1}H NMR (60 MHz, $CDCl_3$) (Me_4Si) δ 0.7–1.3 (m, 24 H), 2.5 (s, 3 H), 2.6 (s, 3 H), 2.0–2.9 (m, 4 H), 4.2–5.8 (b m, 7 H), 7.7 (s, 1 H), 8.1 (s, 1 H), 9.2 (s, 1 H); ^{13}C NMR (62.9 MHz) (Me_4Si) δ 175.6–176.6 (multiple lines), 159.5, 154.7, 150.6, 148.0, 136.9, 135.9, 134.4, 132.5, 131.3, 115.9, 69.9, 68.8 (two lines), 61.6, 44.2, 33.9, 33.8, 33.6, 33.5, 21.2, 18.0–19.2 (multiple lines); UV (HCOOH) λ_{max} 442 (ϵ 9.4 $\times$ 10^3), 380 (ϵ 1.2 $\times$ 10^4), 272 nm (ϵ 2.9 $\times$ 10^4).

(8) N-Oxide **6b**, but not potassium phenolate **8b**, will convert dimer **5a** into **4a** in CH_3CN solution (conditions as in Table I, reaction monitored by C-18 reverse phase LC).

(9) (a) Hemmerich, P.; Prijs, B.; Erlenmeyer, H. *Helv. Chim. Acta* **1959**, *42*, 2164. (b) Hemmerich, P. *Ibid.* **1960**, *43*, 1942. (c) Ehrenberg, A.; Müller, F.; Hemmerich, P. *Eur. J. Biochem.* **1967**, *2*, 286.

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Scheme I

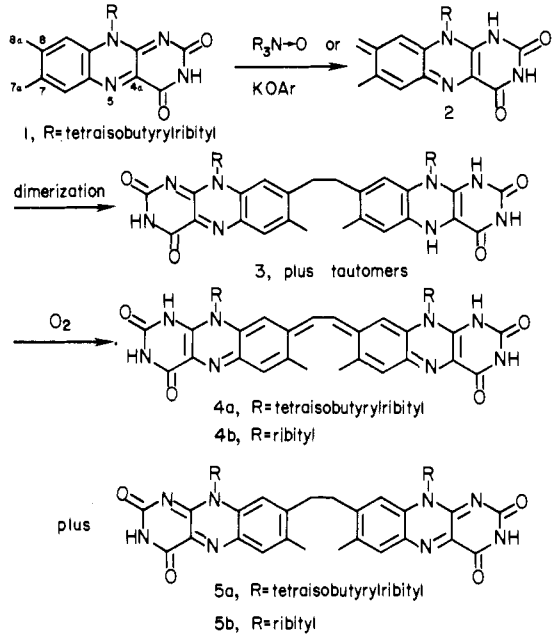


Table I. Dimerization of Tetraisobutyrylriboflavin (1) Using Basic Catalysts

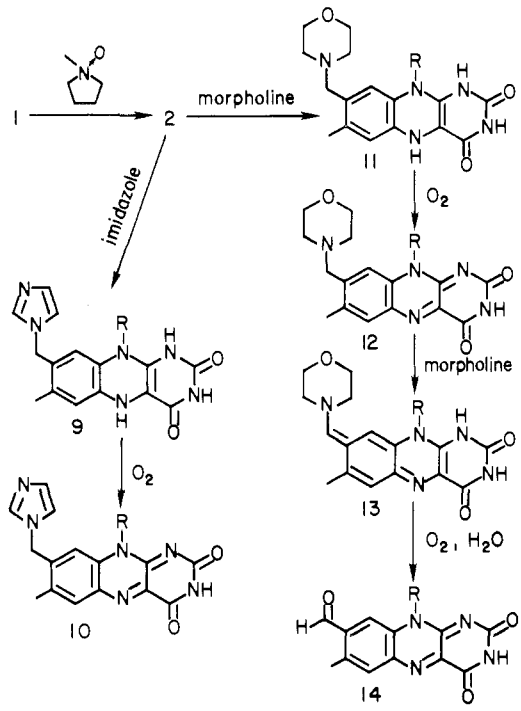
catalyst	conditions[a]	LC yield[b] (%) 4a	5a	1
6a	24 h	10	–	14
6b	24 h	12	–	4
6c	24 h	trace	–	12
7	10 h	20	–	62
8a	6 h	29	19	52
8b	6 h	17	38	42

generation of **4b**[9] with stronger bases under forcing conditions, the capacity of simple *N*-oxides to catalyze the same conversion was unexpected.

A likely mechanism[9a] for dimer (**4**, **5**) formation (Scheme I) has as key intermediate a quinone methide tautomer (**2**) of tetraisobutyrylriboflavin (**1**). *N*-Oxide-catalyzed dimerization of **1** is prevented in the presence of 2,3,5,6-tetramethylphenol. When *O*-deuterio-2,3,5,6-tetramethylphenol is used to inhibit dimerization, recovery of flavin after 24 h reveals (^{1}H NMR) a substantial decrease (~50%) in the intensity of the 8α-methyl absorption relative to the 7α-methyl absorption. Prevention of dimer

(10) Dimer **5b** was also reported by Hemmerich (ref 9a) who noted its conversion into **4b**.

Scheme II



formation by the phenol thus may reflect the protonation of quinone methide (**2**) at the 8α-methylene. Similar deuterium exchange was observed by Bullock and Jardetzky[11] when flavin mononucleotide was heated at 90–95 °C in D_2O at pH 6.8–6.9.

The susceptibility of the quinone methide tautomer (**2**) to nucleophilic attack (e.g., **2** → **9**, Scheme II) is shown by reaction of tetraisobutyrylriboflavin (**1**) with a sixfold excess of both imidazole and *N*-methylpyrrolidine *N*-oxide (**6b**). Reaction at room temperature in dry acetonitrile under anaerobic conditions for 28 h, followed by exposure to the atmosphere, affords yellow-gold, crystalline 8α-imidazolyltetraisobutyrylriboflavin (**10**)[12] (isolated yield 20%, LC yield 28%, plus 32% unreacted **1**, plus 2% **4a**). Nucleophilic interception of the flavin quinone methide (Scheme II) serves as a model for in vivo attachment of flavin to histidine in succinate dehydrogenase.

More complex reactivity is associated with the reaction of tetraisobutyrylriboflavin (**1**) with morpholine (6 equiv) and *N*-methylpyrrolidine *N*-oxide (**6b**, 6 equiv). After reaction under anaerobic conditions (24 h, CH_3CN, ambient temperature), followed by exposure to the atmosphere and chromatography, these components afford orange, crystalline 8-formyltetraisobutyrylriboflavin (**14**)[13,14] in 43% isolated yield (LC yield 82%, plus 4%

(11) Bullock, F. J.; Jardetzky, O. *J. Org. Chem.* **1965**, *30*, 2056.

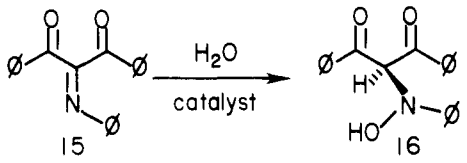
(12) Data for **10**: ^{1}H NMR (60 MHz, $CDCl_3$) (Me_4Si) δ 0.7–1.4 (m, 24 H), 2.4 (s, 3 H), 2.0–2.8 (m, 4 H), 4.0–5.8 (b m, 9 H), 6.9 (s, 1 H), 7.1 (s, 1 H), 7.6 (s, 1 H), 7.7 (s, 1 H), 8.0 (s, 1 H), 10.2 (br s, 1 H); ^{13}C NMR (22.6 MHz, $CDCl_3$) (Me_4Si) δ 176.8, 176.2, 175.9, 175.7, 159.1, 154.8, 150.8, 143.2, 137.9, 137.6, 135.6, 135.2, 134.4, 131.4, 130.0, 119.1, 115.9, 70.6, 69.1, 68.7, 61.9, 49.0, 33.7–33.9 (multiple lines), 18.3–18.8 (multiple lines); IR (KBr) 2975, 1730, 1680, 1580, 1540, 1500, 1450, 1380, 1340, 1230, 1180, 1140, 820, 740, 440 cm^{-1}; UV ($CHCl_3$) λ_{max} 448 (ϵ 1.0 × 10^4), 472 shoulder (ϵ 7.8 × 10^3), 428 shoulder (ϵ 8.3 × 10^3), 336 nm (ϵ 7.6 × 10^3). Anal. Calcd for $C_{36}H_{46}N_6O_{10}$: C, 59.81; H, 6.43; N, 11.63. Found: C, 59.94; H, 6.62; N, 11.42. Field-desorption MS, M$^+$ *m/e* 722.6.

(13) For 8-formylriboflavin and derivatives, see: (a) Edmondson, D. E. *Biochemistry* **1974**, *13*, 2817. (b) McCormick, D. B. *J. Heterocycl. Chem.* **1970**, *7*, 447.

(14) Data for **14**: ^{1}H NMR (60 MHz, $CDCl_3$) (Me_4Si) δ 0.6–1.4 (m, 24 H), 2.8 (s, 3 H), 2.0–2.9 (m, 4 H), 4.0–5.9 (b m, 7 H), 8.1 (s, 1 H), 8.2 (s, 1 H), 9.3 (br s, 1 H), 10.5 (s, 1 H); ^{13}C NMR (22.6 MHz, $CDCl_3$) (Me_4Si) δ 190.5, 175.7–176.6 (multiple lines), 158.6, 154.3, 150.8, 139.8, 138.2, 137.6, 137.4, 135.8, 131.4, 118.0, 69.8, 69.0 (2 lines), 61.8, 43.6, 33.9–34.0 (multiple lines), 18.2–18.9 (multiple lines); IR (KBr) 2980, 1740, 1700, 1615, 1585, 1540, 1460, 1380, 1345, 1235, 1180, 1140, 835, 740, 440 cm^{-1}; UV ($CHCl_3$) λ_{max} 464 (ϵ 1.1 × 10^4), 488 shoulder (ϵ 7.5 × 10^3), 444 shoulder (ϵ 8.9 × 10^3), 340 nm (ϵ 1.2 × 10^4). Anal. Calcd for $C_{33}H_{42}N_4O_{11}$: C, 59.08; H, 6.32; N, 8.35. Found C, 58.87; H, 6.35; N, 8.27. Field-desorption MS, M$^+$ *m/e* 670.6.

unreacted **1**, plus 1% dimer **4a**). The conversion **1** → **14** (Scheme II) may reflect oxidation of the initially formed adduct **11** upon exposure to the atmosphere and further tautomerization (**12** → **13**) of **12** in the presence of excess morpholine. Upon exposure to water and oxygen, **13** would readily give the observed 8-formylated product **14**.[15] The stability of the imidazole adduct **10** to similar workup conditions may reflect the lower basicity of imidazole as compared to morpholine.[16]

The tautomerization **1** → **2** likely proceeds directly by 8α-proton abstraction from **1** (general base catalysis) by the bases of Table I. The rate of flavin dimerization is base dependent (**8b** ≃ **8a** > **7** > **6a** ≃ **6b** > **6c**), paralleling the basicity of the catalysts in organic solvent (see Figure 1).[17] We had considered that an N(5) covalent adduct of **1** with some bases might form competitively with the tautomerization **1** → **2** or alternatively as an intermediate preceding tautomerization. Such an adduct would be stabilized by delocalization of the N(1) dihydroflavin anion (pK_a at N(1) ≃ 6–7).[18] We have examined the reactivity of imine **15** toward the bases of Table I. As a simple model[19] for the flavin N(5)–C(4α) unsaturation, **15** might add bases at nitrogen, at least reversibly, giving a stabilized dibenzoylmethane anion. No adduct formation of **15** with bases was noted; rather hydration of the imine (**15** → **16**[20]) in moist acetonitrile is accelerated by the same



catalysts responsible for flavin dimerization (Table I). A Brønsted plot (Figure 1)[17] for the hydration of **15**, catalyzed by the six bases of Table I, is a straight line indicative of general base catalysis. A striking smilarity of both absolute and relative catalyst activity for imine hydration and flavin dimerization[21] suggests that general base catalysis is a sufficient condition for tautomerization **1** → **2**.

The mild in vitro generation and interception of the flavin quinone methide (**2**) suggests a critical biological role for this long-ignored tautomer. Bases present in vivo may catalyze tautomerization of flavins at flavoenzyme active sites, resulting in the covalent attachment of enzyme and coenzyme. For example, the substrates for monoamine oxidase may play a role in the known attachment of the flavin cofactor to an active-site cysteine residue.[3] Our continuing study of tautomer **2** will focus on the susceptibility of the quinone methide to other nucleophiles from the family of amino acids.

Acknowledgment. This work was generously supported by National Institutes of Health Grant No. CA 20574. We thank Professor Chris Walsh and his research collaborators for stimulating discussions, and Dr. C. Costello for field-desorption mass spectra.

Supplementary Material Available: Brønsted plot for hydration of imine **15** (Figure 1) (1 page). Ordering information is given on any current masthead page.

(15) An alternative mechanism might proceed by addition of the *N*-oxide to tautomer **2** followed by base-mediated 8α-proton abstraction with N–O bond cleavage. This mechanism is unlikely as substitution of the tertiary amine, *N*-methylpyrrolidine, for morpholine (see Scheme II) results in only dimer (**4**) formation with no **14** observable.

(16) Imidazole in the absence of *N*-oxide **6b** does not catalyze flavin dimerization or production of adduct **10**.

(17) Supplementary material.

(18) For a general discussion of flavin covalent adducts, see: Bruice, T. C. *Acc. Chem. Res.* **1980**, *13*, 256.

(19) Use of a similar imine model compound has proven to be useful in studies of flavin-mediated thiol oxidations: Sayer, J. M.; Conlon, P.; Hupp, J.; Fancher, J.; Belanger, R.; White, E. J. *J. Am. Chem. Soc.* **1979**, *101*, 1890.

(20) Scheinbaum, M. L. *Tetrahedron Lett.* **1969**, 4221.

(21) Only some *N*-oxides (e.g., **6a–c**) display catalytic activity for flavin dimerization and imine hydration (**15** → **16**). Inactive catalysts include *N,N*-dimethylaniline *N*-oxide, trimethylamine *N*-oxide, and pyridine *N*-oxide.

(22) Firmenich Assistant Professor of Natural Products Chemistry, Alfred P. Sloan Fellow, 1980–1982.

John W. Frost, William H. Rastetter*[22]
Department of Chemistry
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139
Received July 14, 1980

Induced α Helix in a Peptide System by Introduction of a Nucleus

Sir:

The recent successful estimation of protein structure[1] demonstrates that protein structure is principally determined by the sequence of amino acids with the intrinsic conformational preference. Studies on conformations of model peptide systems having specific sequences of various amino acids are of much interest on this standpoint. We are specially interested in a simple peptide system having the alternating glycine–L-leucine. Glycine is known to be an amino acid which prevents formation of the α helix.[2] On the other hand, L-leucine is classified as an amino acid which strongly tends to form the α helix and thus stabilizes this conformation.[3] Therefore, the conformation of the peptide consisting of L-Leu-Gly sequence should be formed by a counterbalance between opposite conformational preference of these amino acids. We have synthesized a series of peptides shown by Nps-(L-Leu-Gly)$_n$-OEt (n = 1–10)[4] and examined their conformations in the solid state. Because of the strong tendency of L-leucine to form the α helix, we expected to find the α-helical conformation in this peptide system. The conformational study, however, demonstrated that the peptides do not form the α helix but assume the β structure. This result led us to the speculation that if the β structure observed in this series of peptides results actually from the counterbalance of the local conformations of these amino acids, introduction of a nucleus favoring, locally, the α-helical conformation into this peptide chain should induce an α-helical conformation over the peptide chain. In order to develop the nucleus in this peptide system, it may be most effective to insert an additional amino acid sequence having a strong tendency to form the α helix into the original amino acid sequence. We have introduced L-alanyl residues into the peptide chain consisting of the L-Leu-Gly sequence and synthesized Nps-(L-Leu-Gly)$_4$-(L-Ala)$_n$-(L-Leu-Gly)$_4$-OEt (n = 1 and 2).[5] The original and modified sequences of amino acids are shown by

LeuGlyLeuGlyLeuGlyLeuGlyLeuGlyLeuGlyLeuGly-
LeuGlyLeuGlyLeuGly

and

LeuGlyLeuGlyLeuGlyLeuGly*Ala*(*Ala*)LeuGlyLeuGly-
LeuGlyLeuGly

The conformmations in the solid state were examined by infrared (IR) spectroscopy and X-ray powder diffraction measurement. Figure 1 shows the IR spectra of these peptides.[6] The

(1) Chou, P. Y.; Fasman, G. D. *Annu. Rev. Biochem.* **1978**, *47*, 251–276.

(2) Fasman, G. D. "Poly-α-Amino Acids"; Marcel Dekker: New York, 1976; pp 499–604.

(3) Chou, P. Y.; Fasman, G. D. *Biochemistry* **1974**, *13*, 222–245.

(4) Peptide synthesis was done by the fragment condensation method using the active esters Nps-L-Leu-Gly-ONSu and Nps-(L-Leu-Gly)$_2$-ONSu.

(5) These peptides were synthesized from the intermediate peptides Nps-(L-Leu-Gly)$_n$-OEt by the reaction with Nps-L-Ala-L-Leu-Gly-ONSu and Nps-L-Ala-L-Ala-L-Leu-Gly-ONSu.

(6) The amide II band resulting from a deformational vibration of the N–H bonding is also sensitive to the conformational change of peptides and can be used to identify the conformations. However, since the peptides protected by the Nps group show strong bands in the amide II region, the amide II band cannot be used for assignment of the conformation of the Nps peptides.

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