Scheme I

$$\text{D (III, IV, or V)} \xrightarrow{h\nu} \text{D* (singlet)} \quad \text{(a)}$$

$$\text{D* (singlet)} + \text{I} \rightarrow \text{D}^{+\cdot} + \text{I}^{-\cdot} \quad \text{(b)}$$

$$\text{I}^{-\cdot} + \text{H}^{+} \rightarrow (\text{C}_6\text{H}_5)_2\dot{\text{C}}\text{CH}_3 \quad \text{(c)}$$
IX

$$\text{IX} + \text{D}^{+\cdot} \rightarrow (\text{C}_6\text{H}_5)_2\text{C}^{+}\text{CH}_3 + \text{D} \quad \text{(d)}$$
X

$$\text{X} + \text{CH}_3\text{OH} \rightarrow (\text{C}_6\text{H}_5)_2\text{CCH}_3 + \text{H}^{+} \quad \text{(e)}$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad |$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad \text{OCH}_3$$
VI

Step a, excitation of the photosensitizer, is assured by the use of an appropriate filter. Furthermore, no reaction is observed upon irradiation of I under identical conditions except for the absence of a sensitizer.

Step b, which may involve several intermediate stages (exciplex, radical-ion pair, etc.) leads ultimately to the radical ions. The extent to which the radical ions become separated is as yet unknown; however, in this polar medium the calculated coulombic attraction between the ions is quite small (1.3 kcal mol^{-1} at 7 Å separation in acetonitrile). Involvement of the singlet state of the sensitizer (III, IV, or V) is indicated by the fluorescence quenching studies summarized in Table I. The possibility that the triplet state of I is responsible for the observed reaction is ruled out by the observation that 1-benzoylnaphthalene or benzophenone do not sensitize the reaction. Besides, the triplet of I is undoubtedly rapidly deactivated by the free-rotor effect.[5]

An estimate of the free-enthalpy associated with the electron-transfer step can be obtained using eq 3 developed by Weller and coworkers to account for fluorescence quenching by the electron-transfer mechanism.[6]

$$\Delta G \text{ (kcal mol}^{-1}) = 23.06\,[E(\text{D}/\text{D}^{+})_{\text{v}} - E(\text{A}/\text{A}^{-})_{\text{v}} - (e_0^2/\epsilon\alpha)] - \Delta E_{0,0} \text{ (kcal mol}^{-1}) \quad (3)$$

The calculated ΔG values using eq 3 are consistent with the observed reactivity toward addition to the olefin (anti-Markownikoff and Markownikoff): 1-cyanonaphthalene (II) is an effective electron acceptor, the fluorescence of II is quenched by I, eq 3 indicates that the electron-transfer step should be spontaneous, and the anti-Markownikoff addition product formed upon irradiation with this sensitizer is diagnostic of the olefin cation radical. With III, IV, and V, eq 3 indicates that the electron-transfer step should be spontaneous with I as an acceptor, the fluorescence of III, IV, and V is quenched by I, and the Markownikoff addition product is obtained with these sensitizers. The fluorescence quenching rate constants do not correlate with the calculated ΔG values (Table I) which illustrates the importance of factors other than electron transfer for the fluorescence quenching process.[7]

Oxidation of the radical IX by the cation radical of the sensitizer gives the carbocation X (step d). Deprotonation of X should be competitive with reaction with nucleophile (step e) and can account for the observed deuterium incorporation in recovered I.

Step e, reaction of X with methanol should be a general reaction incorporating other nucleophiles. The alcohol VII[4] (68%) was obtained when aqueous acetonitrile was the solvent. When the irradiation was carried out in the presence of potassium cyanide and 2,2,2-trifluoroethanol (a nonnucleophilic proton source) the nitrile VIII[4] (10%) was obtained (reaction 2). The virtue of trifluoroethanol as a nonnucleophilic proton source was evident from the relatively small amount of the trifluoroethyl ethers formed in competition with the nitriles upon irradiation of I with either II or III as sensitizers.

A major portion of the consumed sensitizer (III or IV) can be accounted for as photochemical nucleophilic substitution.[8]

We expect that this type of reaction will be general for aryl olefins (at least) and other nucleophiles and that the mild nonacidic conditions which can be used will offer considerable synthetic utility.[9]

Table I. Fluorescence Quenching of Some Naphthalene Derivatives by 1,1-Diphenylethylene (I) in Acetonitrile Solution at 20 °C

Fluorophor	τ, ns	k_q M^{-1} s^{-1}	ΔG, kcal mol^{-1}, calcd[b]
II	8.923[a]	1.26×10^{10}	−2.8[c]
III	13.6	1.98×10^{9}	−5.7[d]
IV	8.474	4.97×10^{8}	−4.6[d]
V	72.3	1.41×10^{8}	−5.2[d]

[a] Taken from ref 2c. [b] Using eq 3. Details will be reported in the full paper. [c] With I as the donor. [d] With I as the acceptor.

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(3) All irradiations were carried out on argon-purged solutions in Pyrex tubes using a 1-kW medium-pressure mercury vapor lamp (GE Co.) at 10 °C.
(4) Structure based upon comparison (IR, NMR) with authentic samples.
(5) H. E. Zimmerman, F. X. Albrecht, and M. J. Haire, *J. Am. Chem. Soc.*, **97**, 3726 (1975).
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(9) NOTE ADDED IN PROOF. We have learned that E. F. Ullman, C.-I. Lin, and P. Singh have obtained simular results.

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A Model for an Intermediate in Pyridoxal Catalyzed γ-Elimination and γ-Replacement Reactions of Amino Acids

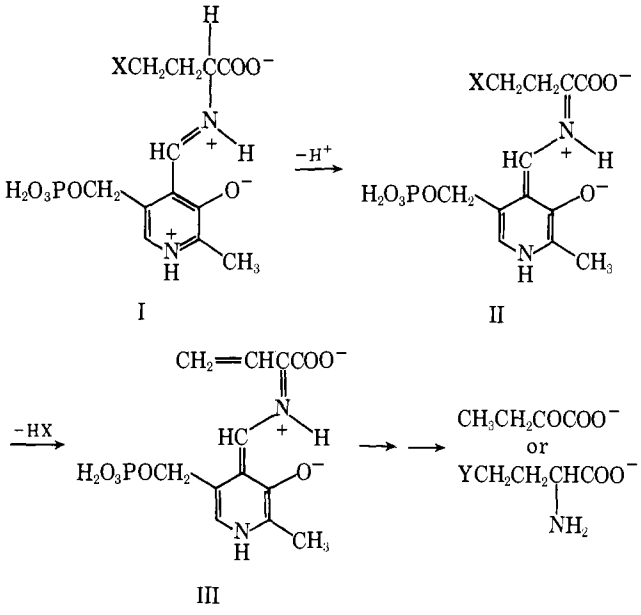
Sir:

Pyridoxal phosphate enzymes catalyze γ-elimination and γ-replacement reactions of amino acids and the reactions have been proposed to proceed through a series of Schiff base intermediates shown in Scheme I.[1-3] This report describes a spectral model for intermediate III.

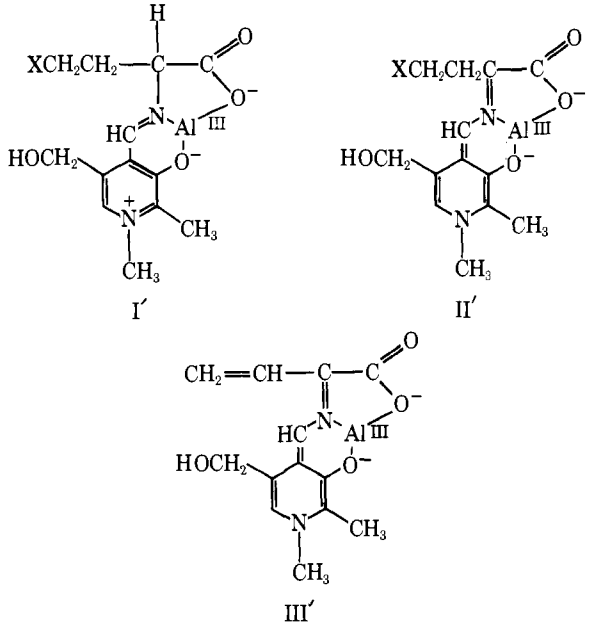
A number of enzymatic and nonenzymatic studies have established that intermediates I and II absorb at ~420 and 500 nm, respectively.[2-4] Intermediate III has been predicted to absorb above 500 nm, since it has an extended conjugate system.[2] Miles[3] suggested that a transient absorption at 510 nm observed during tryptophan synthase catalyzed reaction of *trans*-L-2-amino-4-methoxy-3-butenoic acid might result from this structure.

Pyridoxal *N*-methochloride (1×10^{-4} M) and 2-aminobutanoic acid (1×10^{-3} M) were mixed in slightly alkaline

Scheme I



Scheme II



methanol (KOH, 2×10^{-3} M). After 1 h a methanolic solution of aluminum nitrate (1×10^{-4} M) was added. The spectrum of the solution had a peak at 388 nm, which decreased its intensity with the appearance of an absorption at 514 nm. From the previous results,[4] the 388- and 514-nm absorption can be assigned to the aluminum(III) chelates of the aldimine (I′, X = H, Scheme II) and of the quinoid intermediate (II′, X = H), respectively.

The replacement of 2-aminobutanoic acid by 2-amino-3-butenoic acid in the reaction, however, produces an absorption at 550 nm instead of that at 514 nm. The result suggests the 550-nm absorption can be assigned to the aluminum(III) chelate III′. The aluminum(III) chelate of the Schiff base derived from an α,β-unsaturated amino acid should absorb at the shorter wavelength region.[5]

To an alkaline methanol solution (KOH, 2×10^{-3} M) containing pyridoxal *N*-methochloride (1×10^{-4} M) and methionine (1×10^{-3} M), aluminum nitrate (1×10^{-4} M) and 2-mercaptoethanol (1×10^{-2} M) were added. Figure 1 shows the spectral change observed in this system at room temperature. Initial rapid spectral change consisted of a decrease of the 388-nm peak and the appearance of the 514-nm band. The absorbance at 514 nm reached its maximum 2 min after the addition of aluminum(III). With a decrease of the 514-nm band, developed a new absorption at 550 nm similar to that observed in the pyridoxal *N*-methochloride–2-amino-3-butenoic acid–aluminum(III) reaction. The 550-nm absorbance reached its maximum in 4 h and then decreased gradually. Finally the spectrum had a peak at 348 nm, showing the presence of a ketimine derived from 1-methylpyridoxamine chloride.

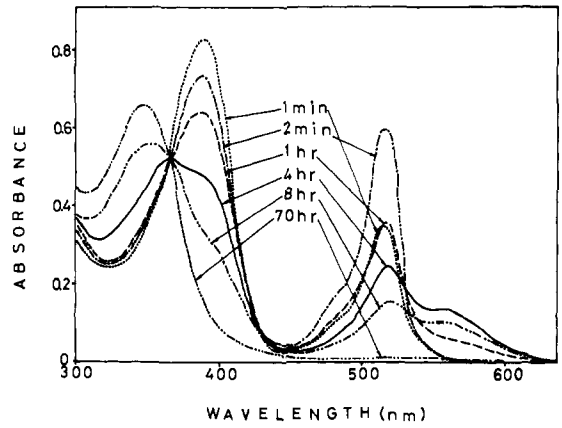


Figure 1. Spectral change accompanying the reaction of pyridoxal *N*-methochloride, methionine, 2-mercaptoethanol, and aluminum(III) nitrate in methanol. Concentrations in the final mixture are given in the text. Times after initiating the reaction are indicated beside the spectral curves.

The spectral change suggests the aluminum(III) chelate catalyzed γ-elimination or γ-replacement reaction of methionine. The replacement of methionine by methionine sulfoxide, methionine sulfone, ethionine, ethionine sulfoxide, and *S*-phenylhomocysteine in the system gave similar results. Valine, norvaline, leucine, and *S*-methylcysteine failed to produce the 550-nm absorption under the conditions. 1-Methyl-3-hydroxy-4-formylpyridinium chloride can replace pyridoxal *N*-methochloride, while pyridoxal and 3-hydroxy-4-formylpyridine can not, for the generation of the absorption. Use of gallium(III) in the place of aluminum(III) resulted in the formation of a species of the same spectral character. The 550-nm absorption disappeared with the addition of tetrasodium ethylenediaminetetraacetate, which suggests the absorption is ascribable to aluminum(III) chelate.

The absorption was also formed when thiophenol was used in the place of 2-mercaptoethanol. In the absence of the thiols a small absorption was formed at ~550 nm with methionine sulfone, but not with methionine. The thiols seemed to intensify the bands at 514 and at 550 nm.

To an alkaline methanol solution (KOH, 20 mmol) containing pyridoxal *N*-methochloride (2 mmol) and methionine sulfone (2 mmol), aluminum nitrate (2 mmol) and thiophenol (100 mmol) were added. After 3 h at room temperature, pyridoxamine (3 mmol) and zinc nitrate (10 mmol) were added and the mixture was allowed to stand for 2 days. *S*-Phenylhomocysteine was separated from the reaction mixture. The result suggests that the γ substituent of the amino acid was replaced nonenzymatically.

On the grounds mentioned above, we conclude that the 550-nm absorption can be assigned to structure III′ and may serve as a model for intermediate III in enzymatic reactions.

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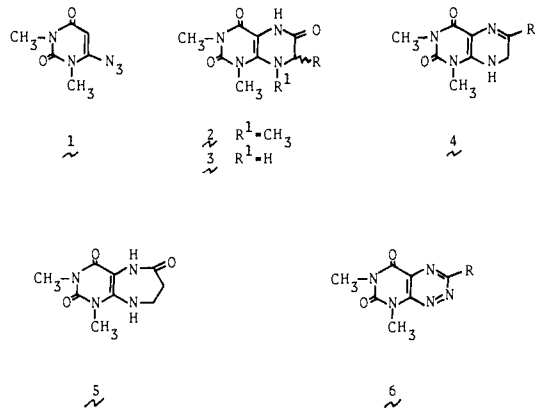
A New Photochemical Synthesis of Lumazines and Fervenulins from 6-Azido-1,3-dimethyluracil

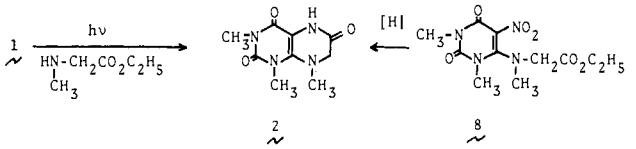
Sir:

We recently described that the photolysis of 6-azido-1,3-dimethyluracil (**1**) in the presence of primary or secondary alkylamines led to the formation of 6-alkylamino-5-amino-1,3-dimethyluracils in high yields via a nitrene intermediate.[1] This photochemical transformation (6-N_3 → 5-NH_2) is a new type of procedure to introduce a nitrogen source into the 5 position of the uracils as compared with conventional methods, i.e., nitration, nitrosation, or the Michael-type addition of diethyl azodicarboxylate.[2]

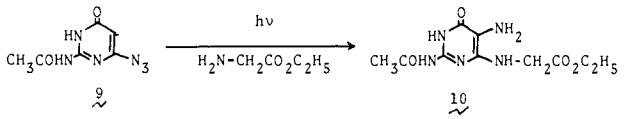


During studies directed toward the development of new synthetic routes to heterocycles employing 6-azidouracils, we have succeeded in obtaining lumazines and fervenulins in a single step and, furthermore, in high yields using amino acid esters, amino ketones, and acylhydrazines in place of alkylamines in the above reaction.

Scheme I



Scheme II



Thus, a mixture of **1** (0.011 M) and *N*-methylglycine ethyl ester (0.033 M) in THF was irradiated[3] for 3 h and the solvent was removed by evaporation. Trituration of the residue with ether gave 7,8-dihydro-1,3,8-trimethyllumazin-6(5*H*)-one (**2**) (Scheme I) in 73% yield: mp 240–241 °C; IR (KBr) 3170 cm^{-1} (NH); UV λ_{max}^{EtOH} 245 nm (log ϵ 6.1), 262 (5.9, sh), 313 (5.9); NMR ($CDCl_3$) δ 2.90, 3.44, and 3.48 (each 3 H, each s, each *N*-CH_3), 3.78 (2 H, s, $COCH_2N$), 8.49 (1 H, br s, NH, deuterium exchangeable). The identification of structure **2** was established by an alternate synthesis[4] of this compound from 6-chloro-1,3-dimethyl-5-nitrouracil (**7**).[5] Thus, treatment of **7** with *N*-methylglycine ethyl ester gave 1,3-dimethyl-6-(*N*-ethoxycarbonylmethyl-*N*-methyl)amino-5-nitrouracil (**8**). Reductive ring closure of **8** by catalytic hydrogenation afforded the lumazine (**2**) which was identical with the product obtained by photolysis of **1**.

Similar irradiation of **1** (0.011 M) and other various amino acid ethyl esters efficiently gave the corresponding 7-substituted lumazin-6-ones (**3a–d**)[6] in good yields. On the irradiation of **1** with β-amino ketones, 6-substituted lumazines (**4a,b**) were obtained (see Table I).

We also used 2-acetylamino-6-azidopyrimidin-4(3*H*)-one (**9**) instead of **1** for this reaction. Irradiation of **9**[7] with glycine ethyl ester in THF for 5 h and the resulting precipitate being collected by filtration gave 2-acetylamino-5-amino-6-(*N*-ethoxycarbonylmethyl)aminopyrimidin-4(3*H*)-one (**10**) (Scheme II), mp 213–214 °C, in quantitative yield. Although the predicted cyclization to a pterin did not occurr, the pyrimidone **10** is a potential intermediate for 6-hydroxypterin.[8]

Furthermore, when a solution of **1** and β-alanine ethyl ester in THF was irradiated, 7,8-dihydro-1,3-dimethyl-9*H*-pyrimido[4,5-*b*]-5,9-diazepine-2,4,6(1*H*,3*H*,5*H*)-trione (**5**) was obtained in 59% yield: mp 200–201 °C; UV λ_{max}^{EtOH} 267 nm (log ϵ 4.9), 297 (5.0); NMR (DMSO-d_6) δ 2.60 (2 H, m,

Table I. Photochemical Formation of Lumazines

Amino acid ethyl ester or amino ketone	Product	R	Mp, °C	Yield, %
Glycine ethyl ester	**3a**	H	285	69
Alanine ethyl ester	**3b**	CH_3	270	76
Phenylalanine ethyl ester	**3c**	$C_6H_5CH_2$	223–225	55
Methionine ethyl ester	**3d**	$CH_3S(CH_2)_2$	197–200	61
Phenacylamine	**4a**	C_6H_5	255–257	75
p-Bromophenacylamine	**4b**	*p*-BrC_6H_4	260–262	70

Table II. Photochemical Formation of 3-Substituted Fervenulins

Acylhydrazine	Product	R	Mp, °C	Yield, %
Formylhydrazine	**6a**	H	174–175	55
Acetylhydrazine	**6b**	CH_3	124–126	68
Benzoylhydrazine	**6c**	C_6H_5	278–279	81
Phenylacetylhydrazine	**6d**	$C_6H_5CH_2$	190–192	72
Isonicotinoylhydrazine	**6e**	4-Pyridyl	260–262	60