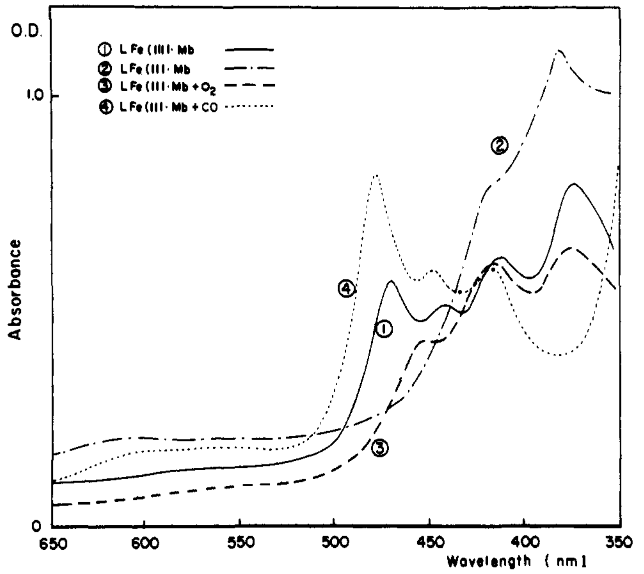

Figure 6. The visible spectra of the Fe(III) and Fe(II) complexes with apomyoglobin, and the interaction of Fe(II) bound myoglobin complex with O_2 and CO.

shown to be the heme site in hemoglobin.[13] Similar results have been obtained with apomyoglobin.

The binding of O_2 and CO to apomyoglobin bound complex was examined spectrophotometrically. The electronic absorption spectra of the bound complex after reduction with dithionite is shown in Figure 6. Exposure of the solution to air leads to an electronic absorption spectrum which differs considerably from that of the Fe(III) bound complex. It is suggested that this electronic spectrum results from binding of O_2 to Fe(II). This suggestion is strongly supported by the spectral changes which occur with carbon monoxide. When the reduction is performed in CO atmosphere, the spectrum of the CO adduct is obtained (Figure 6). On exposure of this solution to air, the electronic spectrum reverts to that of the O_2 adduct. This process is irreversible in that the dioxygen molecule can not be displaced with CO. Attempts to remove O_2 by freeze-thaw techniques were so far unsuccessful because of denaturation of the protein. However, it should be pointed out that, although the hydrophobic cavity of the protein prevents the oxidation of the iron complex, the O_2 binding to this particular complex need not be reversible, since the reversibility depends primarily on the electronic structure of the complex.

We are currently studying other iron complexes as well as their cobalt analogues in order to shed more light on this interesting problem.

Acknowledgment. We thank Professor H. B. Gray for helpful discussions and the United States-Israel Binational Science Foundation (BSF) for financial support.

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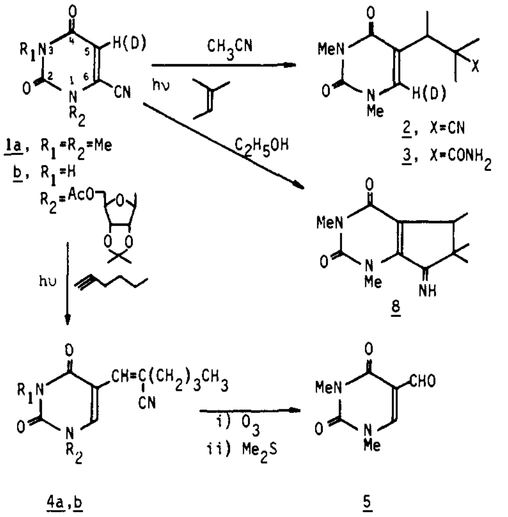
A Novel Photoaddition of 6-Cyanouracils to Alkenes and Alkynes Involving Migration of a Cyano Group[1]

Sir:

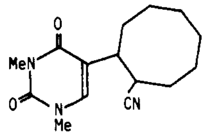
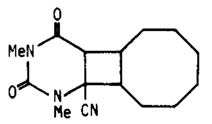
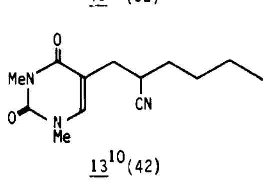
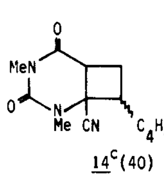
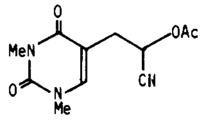
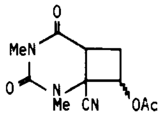
Photochemical cycloaddition of cyclic enones to olefins has been studied for many years from mechanistic and synthetic points of view.[2,3] Recently, Swenton and co-workers have described the remarkable effect of α substituents in controlling the regioselectivity of the photocycloadditions of uracils[4] and cycloalkenones[5] to olefins.[6] During our studies directed toward the photochemical synthesis of nucleic acid–amino acid adducts,[7] we have found that 6-cyanouracils undergo an unusual photoaddition to alkenes and alkynes leading directly to 5-substituted uracils via the migration of the cyano group. The present reaction provides a novel type of photoaddition that can compete with [2 + 2] cycloaddition through a biradical intermediate, and constitutes a new concept for the direct functionalization at the C-5 position of uracil and uridine derivatives.[8]

Irradiation of 6-cyano-1,3-dimethyluracil[9] (**1a**, 1 mM) in acetonitrile at 20 °C in the presence of 2-methyl-2-butene (20 mM) with a high-pressure mercury lamp (Pyrex filter) followed by preparative TLC produced a rearranged adduct, **2** (60%). The structure of **2** was assigned on the basis of spectral data[10] and by converting it into the amide **3**[10] (50%, AcOH–H_2SO_4). Irradiation of **1a** with 1-hexyne in acetonitrile under the same conditions gave a 1:1 *E*-*Z* mixture of **4a**[10] (65%).[11] Both isomers produced 5-formyl-1,3-dimethyluracil[12] (**5**, 55%) upon ozonolysis. In none of these cases was the cycloadduct detected in the reaction mixture.[13] This novel photoaddition was also successfully applied to a 6-cyanopyrimidine nucleoside. Thus, irradiation of **1b**[9] in acetonitrile in the presence of 1-hexyne followed by preparative TLC yielded **4b**[10] (37%).



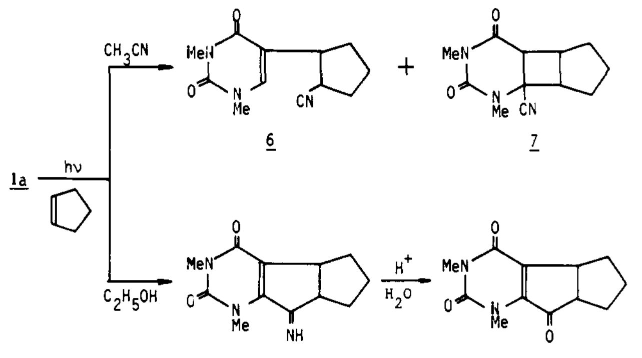
Irradiation of **1a** with other olefins under similar conditions gave the corresponding 5-substituted uracils but in competition with the formation of cycloadducts (Table I) with the ratio of the products being temperature dependent. For example, ir-

Table I. Photoaddition of 6-Cyano-1,3-dimethyluracil (**1a**) to Olefins in Acetonitrile[a]

olefin	products (%, yield[b])	
cis-cyclooctene	 11[10] (52)	 12[c] (35)
1-hexene	 13[10] (42)	 14[c] (40)
vinyl acetate	 15[10] (10)	 16[c] (60)

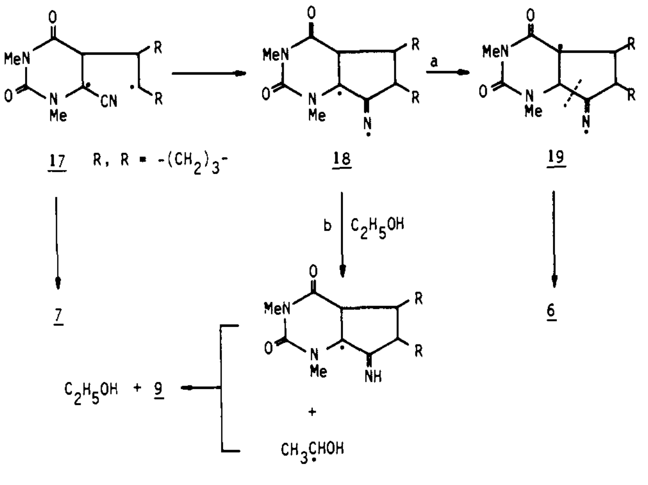
[a] Conditions: [**1a**] = 1 mM; [olefin] = 20 mM, at 20 °C. [b] Isolated yield. [c] Inseparable mixture of two stereoisomers.

radiation of **1a** (1 mM) with cyclopentene (20 mM) in acetonitrile at 20 °C gave the rearranged adduct **6**[10] (43%) and cyclobutane **7**[14] (26%), whereas **7** (56%) was formed as the major product with a minor amount of **6** (15%) upon irradiation at −20 °C. The irradiation in alcohols, however, produced a different product. Irradiation of **1a** with 2-methyl-2-butene in ethanol at 20 °C gave **8**[10] (80%) as a single photoproduct. Similarly, irradiation of **1a** with cyclopentene in ethanol at 20 °C yielded **7** (20%) and **9** which on workup produced **10**[10] (50%), whereas the cyclobutane **7** (70%) was again the sole isolable product upon photolysis at −78 °C. Thus the results demonstrate an unique example in which photoadducts are controlled by temperature and solvent. A similar type of photorearrangement that can compete with [2 + 2] cycloaddition at elevated temperature has recently been reported by Agosta.[16] The photoreaction of **1a** with cyclopentene was sensitized by xanthone in acetonitrile and the products **6** and **7** were formed in approximately the same yield.[17]



All of the experimental results may be most reasonably rationalized by assuming a biradical intermediate of the sort generally implicated in [2 + 2] photocycloaddition,[2-4] although information on the mechanistic details is minimal. The biradical intermediate **17**, a common precursor for all products, may close to bicyclic iminium species **18** (Scheme I). This species can undergo a 1,2 hydrogen shift to **19** (path a), and subsequent β cleavage of the biradical **19** could then furnish the rearranged adduct **6**.[18] In ethanol the biradical intermediate **18** abstracts a hydrogen from the solvent followed by disproportionation to give **9** (path b).[19] The remarkable temperature effect on the product ratio is also explicable by assuming that the cyclization of **17** to **18** requires thermal activation; i.e., the cyclization becomes more feasible with increasing temperature.[20] A similar 1,4 migration of a cyano group has reasonable precedent in free-radical reactions.[16b,21] We are unaware, however, of any previous example in which the transfer of a cyano group has been observed during the intermolecular [2 + 2] photocycloaddition.

Scheme I



The present work described here provides a useful synthetic method for appending a functionalized chain of arbitrary length to the C-5 position of the uracil nucleus. Furthermore, the powerful effect of a cyano group on the regioselectivity coupled with the unique migration of cyano group observed here may suggest further utility of α,β-unsaturated nitriles in the [2 + 2] photocycloaddition reactions. We are continuing to explore the scope and mechanistic details of this novel photoreaction.

Acknowledgment. This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education of Japan and the Yamada Science Foundation. The authors are grateful to Kyowa Fermentation Co., Ltd., for a generous gift of uridine.

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(9) (a) Inoue, H.; Ueda, T. *Chem. Pharm. Bull.* (*Tokyo*) **1971,** *22*, 1179. (b) Senda, S.; Hirota, K.; Asao, T. *J. Org. Chem.* **1975,** *40*, 353. **1a**: UV (CH_3CN) 289 nm (log ϵ 3.89).
(10) All new compounds exhibited consistent spectral data (^1H and ^{13}C NMR, UV, IR, MS) and elemental analyses. Selected spectral data follow. **2:** mp 119–120 °C; ^1H NMR ($CDCl_3$) δ 1.26 (s, 3 H), 1.32 (d, J = 7.2 Hz, 3 H), 1.46 (s, 3 H), 3.16 (q, J = 7.2 Hz, 1 H), 3.36 (s, 3 H), 3.44 (s, 3 H), 7.32 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 16.6, 25.1, 25.8, 28.1, 36.4, 37.0, 38.5, 114.1, 123.6, 140.3, 150.9, 163.5; UV (CH_3CN) 271 nm (log ϵ 3.90; MS (70 eV) *m/e* 235 ($M^{\dagger}$), 167, 110, 69. **3:** mp 172–175 °C; ^1H NMR ($CDCl_3$) δ 1.15 (s, 3 H), 1.19

(s, 3 H), 1.20 (d, J = 7.5 Hz, 3 H), 3.31 (q, J = 7.5 Hz, 1 H), 3.34 (s, 3 H), 3.40 (s, 3 H), 6.00 (br, 2 H, NH_2), 7.11 (s, 1 H). (*E*)-**4a**: syrup; ^{1}H NMR (CCl_4) δ 0.96 (t, J = 6.5 Hz, 3 H), 1.16–1.74 (m, 4 H), 2.36 (t, J = 7 Hz, 2 H), 3.25 (s, 3 H), 3.46 (s, 3 H), 6.95 (br s, 1 H), 8.23 (s, 1 H); UV (CH_3CN) 313 nm (log ϵ 4.05), 259 (3.92). (*Z*)-**4a**: *syrup*; ^{1}H NMR (CCl_4) δ 0.95 (t, J = 6.6 Hz, 3 H), 1.22–1.76 (m, 4 H), 2.32 (t, J = 7 Hz, 2 H), 3.25 (s, 3 H), 3.42 (s, 3 H), 6.86 (br s, 1 H), 7.44 (s, 1 H); UV (CH_3CN) 303 nm (log ϵ 4.02), 258 (3.79). **4b**: syrup; ^{1}H NMR ($CDCl_3$) δ 1.33 (t, J = 7 Hz, 3 H), 1.76 (s, 3 H), 1.98 (s, 3 H), 1.60–2.10 (m, 4 H), 2.46 (s, 3 H), 2.75 (t, J = 7 Hz, 2 H), 3.65–3.80 (m, 1 H), 3.76 (d, J = 1 Hz, 2 H), 4.18–4.26 (m, 1 H), 4.38 (dd, J = 6, 2 Hz, 1 H), 5.30 (d, J = 2 Hz, 1 H), 6.42 (s, 1 H), 7.76 (s. 1 H), 9.50 (br, 1 H, NH); judging from the chemical shifts of the olefinic (δ 6.42) and C-6 (δ 7.76) protons, **4b** appears to be *Z* isomer. **6**: viscous oil; ^{1}H NMR ($CDCl_3$) δ 1.80–2.18. (m, 6 H), 3.08–3.22 (m, 1 H), 3.36 (s, 3 H), 3.42 (s, 3 H), 3.5–3.6 (m, 1 H), 7.15 (s, 1 H). **8**: mp 119–120 °C; ^{1}H NMR ($CDCl_3$) δ 1.10 (s, 3 H), 1.15 (s, 3 H), 1.21 (d, J = 7 Hz, 3 H), 2.28 (q, J = 7 Hz, 1 H), 3.36 (s, 3 H), 3.82 (s, 3 H), 9.90 (br s, 1 H, NH); UV (CH_3CN) 306 nm (log ϵ 3.88). **10**: mp 107–108 °C; ^{1}H NMR ($CDCl_3$) δ 1.40–2.10 (m, 6 H), 2.80–3.20 (m, 1 H), 3.38 (s, 3 H), 3.66 (s, 3 H), 3.40–3.60 (m, partially obscured, 1 H); UV (CH_3CN) 313 nm (log ϵ 3.82), 249 (3.27). **11**: viscous oil; ^{1}H NMR ($CDCl_3$) δ 1.30–2.20 (m, 12 H), 2.90–3.30 (m, 2 H), 3.30 (s, 3 H), 3.36 (s, 3 H), 7.06 (s, 1 H). **13**: viscous oil; ^{1}H NMR (CCl_4) δ 0.95 (t, J = 6 Hz, 3 H), 1.20–1.80 (m, 6 H), 2.12–3.00 (m, 3 H), 3.24 (s, 3 H), 3.36 (s, 3 H), 7.24 (s, 1 H). **15**; viscous oil; ^{1}H NMR ($CDCl_3$) δ 2.20 (s, 3 H), 2.95 (d, J = 7 Hz, 2 H), 3.35 (s, 3 H), 3.42 (s, 3 H), 5.58 (t, J = 7 Hz, 1 H), 7.26 (s, 1 H).

(11) Both isomers of **4a** are interconvertible under the irradiation conditions.

(12) Alcántara, R.; Wang, S. Y. *Photochem. Photobiol.* **1965**, *4*, 465.

(13) A considerable amount of polymeric products derived from the olefin and 1-hexyne has been detected. In the absence of olefins **1a** undergoes photodimerization.

(14) A mixture of two stereoisomers. The major isomer was isolated in a pure crystalline form: mp 89–90 °C; ^{1}H NMR ($CDCl_3$) δ 1.60–2.20 (m, 6 H), 2.80–3.20 (m, 2 H), 3.08 (d, J = 6 Hz, 1 H), 3.02 (s, 3 H), 3.22 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 24.3, 27.4, 28.8, 30.5, 31.6, 41.8, 41.9, 47.5, 53.1, 114.9, 150.8, 166.5; IR (Nujol) 1710, 1660 cm^{-1}. This compound did not epimerize upon prolonged exposure to basic alumina, suggesting that the 6–4 *ring* fusion is cis.[15] Attempts to purify the minor isomer have been unsuccessful.

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(16) (a) Barany, F.; Wolff, S.; Agosta, W. C. *J. Am. Chem. Soc.* **1978**, *100*, 1946. (b) Wolff, S.; Agosta, W. C. *J. Org. Chem.* **1978**, *43*, 3627.

(17) Irradiation was done with a 450-W high pressure Hg lamp at 20 °C through a 0.4 M stannous chloride filter solution (cutoff 320 nm).[5b] Under these conditions >95% of the incident light was absorbed by the sensitizer.

(18) Alternative mechanism involving a carbene intermediate derived from **18** appears to be less likely since alcohols should trap such intermediates. In support of the proposed mechanism, irradiation of 5-deuterated **1a**[9b] (90% D) with cyclopentene (3 equiv mol) in $CHCl_3$ provided the 6-deuterio derivative of **6** (55% D). However, a considerable amount of the deuterium of **1a**-d_1 was lost during the photoaddition. Mechanistic studies including trapping experiments of the intermediate are in progress.

(19) The mechanism of the formation of **9** is not clear at this time. Other interpretations are certainly possible.

(20) Conformational change of the biradical **17** by increasing temperature is possibly responsible for this process. A similar temperature-dependent photorearrangement has been observed with geranonitrile; see ref 16b.

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Two-Laser Multiphoton Dissociation of Iodobenzene Cation

Sir:

The simultaneous irradiation of gas-phase iodobenzene ions with 610-nm visible light and 10-μ infrared light results in photodissociation of the ions at a rate strikingly faster than the photodissociation observed with either laser used separately. This simultaneous visible-infrared process has important implications for the nature of multiphoton events and relaxation processes in gas-phase species, and may represent the first observation of a combined visible-IR multiphoton dissociation.

Gas-phase ionic molecules offer a uniquely attractive opportunity for study of multiphoton photochemistry, because of the ease of trapping ions under collision-free or collisional conditions for periods of many seconds or longer. The Penning ion trap with ion cyclotron resonance detection has proven to be a powerful approach to exploiting these possibilities.[1,2]

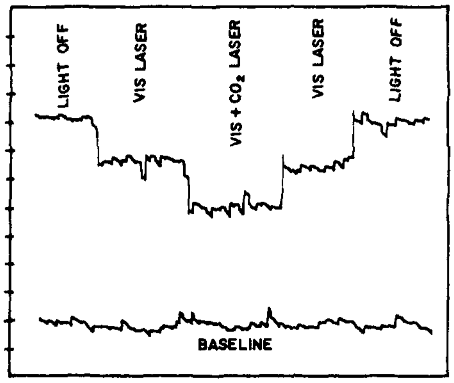

Figure 1. Recorder trace of the pulsed-ICR-detected parent-ion abundance. The time between ion formation and ICR detection is 2.0 s, during which period the ions are irradiated by no light, by either laser alone, or by both lasers, as indicated.

Two notable types of multiphoton processes have been studied for ions: the sequential two-photon (and multiphoton) photodissociation of cations at visible wavelengths with light sources of modest power,[3-5] and multiphoton infrared photodissociation of ions using CW CO_2[2,6,7] lasers. The two-photon visible-wavelength photodissociation of iodobenzene radical cation has been previously described.[8] In the work reported here, visible irradiation was provided by a Chromatix pulsed dye laser operated at 610 nm (which is near the two-photon peak) and at pulse rates between 5 and 30 pulses/s.[9] Dissociation using only the visible laser shows characteristics of pressure dependence and light-intensity dependence consistent with the accepted sequential two-photon dissociation model.

Used alone, the CO_2 laser (unfocussed CW, up to ~10-W/cm^2 power) gave no observable dissociation, but the combination of visible and IR irradiation gave the greatly enhanced dissociation shown in Figure 1. The wavelength dependence of the IR enhancement in the 10-μ region of visible two-photon photodissociation is shown in Figure 2. IR irradiation in the region around 9.6 μ gave little or no enhancement, so that the IR wavelength dependence evidently reflects a broad maximum at ~10.2 μ. Such a broad IR peak, lying in a spectral region where iodobenzene neutral has several absorption peaks, is consistent with IR absorption by a vibrationally excited iodobenzene ion.[10]

At fixed IR intensity, the visible intensity dependence of photodissociation is somewhat stronger than linear, but much weaker than quadratic. The IR intensity dependence is weaker than linear as shown in Figure 2. The pressure dependence is strong at low pressure, but becomes weaker at high pressure (the extent of dissociation decreasing with increasing pressure).

We believe these observations can be understood by considering the behavior of an ion under IR irradiation at modest power: the absorption of IR photons into the resonant normal mode, pumping the ion to higher vibrational energy, is balanced by energy relaxation by collision and by IR radiation. The relevant characteristics of all three of these processes are known or can be estimated,[11-13] and modeling indicates that a balance is rapidly established between excitation and relaxation such that the ion is maintained within a reasonably narrow energy range. It has little chance of falling back near the ground state and has also little chance of exceeding a characteristic maximum energy which increases with increasing IR intensity.[14] Such IR pumping has a marked effect on the two-photon photodissociation process: when an ion