73 (25), 69 (19), 67 (15), 61 (20), 57 (35), 55 (17), 53 (12), 45 (26).

Anal. Calcd for $C_{12}H_{18}N_2O_4$: C, 56.68; H, 7.14; N, 11.02. Found: C, 56.69; H, 6.91; N, 10.95.

N-(β-D-Ribofuranosyl)tetrahydrobenzimidazole (14b). A solution of **13b** (160 mg, 0.52 mmol) in 2 mL of 10% aqueous acetic acid was heated for 6 h at 100 °C. The solution was concentrated to an oil, and the oil was dissolved twice in 2 mL of H_2O and twice in 2 mL of ethanol and concentrated to dryness each time. The residual gum was chromatographed on silica gel and eluted with $CHCl_3$:CH_3OH (9:1) to give 70 mg (50%) of **14b** which could not be obtained crystalline: UV max (CH_3OH) 225 nm; ^1H NMR (Me_2SO-d_6) δ 1.72 (m, 4, 2 CH_2), 2.50 (m, 4, 2 CH_2), 3.57 (d, 2, CH_2), 4.03 (m, 3, 3 CH), 5.05 (br s, 3, 3 OH), 5.42 (d, 1, J = 6 Hz, CH), 7.77 (s, 1, CH); mass spectrum (70 eV), m/e (rel intensity) 254 (10), 149 (19), 123 (23), 122 (97), 121 (11), 94 (87), 73 (23), 69 (10), 67 (15), 61 (15), 60 (57), 57 (24), 55 (15), 46 (13), 45 (100).

Photolysis of (2,3,4-Tri-O-acetylribopyranosyl)diaminomaleonitrile (15) and Ribopyranosyldiaminomaleonitrile.[5] A 2×10^{-3} M solution of **15** (90 mg) in acetonitrile was irradiated with a 300-nm light source in a Pyrex vessel for 41 h. The solvent was removed on a rotary evaporator, and the products were separated by preparative TLC using 5:1 benzene:ethyl acetate. Seven UV-absorbing areas could be detected on the TLC plate. The bands were eluted and their UV spectra were measured in CH_3OH. One of the substances (6 mg) was tentatively identified as **16** on the basis of the comparison of its UV maxima (264 and 225 nm) with those of 1-isopropyl-4-(aminoimidazole)-5-carbonitrile: UV max (CH_3OH) 265, 227 nm.[1] A second substance (6 mg) was tentatively identified as **17** on the basis of the similarity of its UV maxima (257, 228 nm) with those of **16** above. The same compounds were observed in about the same yield when the photolysis was performed with a 350-nm light source in a Pyrex vessel for 144 h. No products with UV absorption in the 250–270-nm region could be detected on irradiating ribosyldiaminomaleonitrile[5] with 300- or 350-nm light sources in a Pyrex vessel. Colored solutions and precipitates were formed, but the UV spectrum of the solution indicated only the presence of starting material.

Acknowledgment. We thank Dr. E. A. Williams for measuring the ^{13}C NMR spectra of **9a** and **9b** and Mr. G. Brooks for technical assistance. This work was supported by Grant No. CA 14511 from the National Cancer Institute and a Project Seed Grant from the American Chemical Society to G. Brooks.

Registry No. **7**, 4513-77-3; **8**, 46167-41-3; **9a**, 71734-86-6; **9b**, 71734-87-7; **13a**, 71734-88-8; **13b**, 71734-89-9; **14a**, 71734-90-2; **14b**, 71734-91-3; **15**, 70042-25-0; **16**, 71734-92-4; **17**, 71734-93-5; ribopyranosyldiaminomaleonitrile, 71772-49-1.

Mechanism of the Photochemical Bleaching of Cyclic Enamino Nitriles

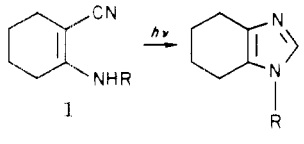
J. P. Ferris,* V. Ramachandra Rao, and T. A. Newton

Department of Chemistry, Rensselaer Polytechnic Institute, Troy, New York 12181

Received August 9, 1979

Photolysis of enamino nitriles in alcohol solution results in the formation of adducts with no UV absorption. These bleached products are thermally labile and regenerate the enamino nitrile grouping. Photolysis of *N*-(2,3-*O*-isopropylidene-α-D-ribofuranosyl)-1-amino-2-cyanocyclohexene (**3a**) yields isomers of the methyl ether **6**. Ether **6** loses methanol at room temperature to regenerate **3a** and its C-1′ isomer **3b**. The presence of isomers of **6** was established by the presence of four overlapping methoxyl peaks in the ^1H NMR spectrum of the photolysate. The anomerization at C-1′ is a thermal reaction which proceeds after **6a** is formed. The presence of compounds isomeric at C-1 was established by the formation of only **3a** and **3b** as a result of elimination of methanol from the isomers of **6**. The methanol addition reaction is not catalyzed by acid or base but does proceed from the triplet excited state as shown by triphenylene-sensitized formation of **6**. The absence of methanol addition to the acyclic β-aminocrotononitrile (**10**) is consistent with the high-energy triplets of the cyclic enamino nitriles **1** and **3** as the intermediates leading to the alcohol addition products. The detection of the ketenimine chromophore at 2030 cm^{-1} on irradiation of **1d** under conditions where rapid alcohol addition to the triplet is observed suggests that the ketenimine is formed via the singlet excited state. Since the photochemical rearrangement of enamino nitriles to imidazoles proceeds from the singlet excited state, these data provide further support for the proposal that an iminoketenimine (e.g., **5a**) is the initial product formed from the singlet enamino nitrile. This ketenimine undergoes thermal transformations to yield the rearranged imidazoles.

The photorearrangement of enamino nitriles is a key step in one of the pathways proposed for prebiological purine synthesis from HCN,[1] and it is an efficient synthetic route to imidazoles (e.g., **1** → **2**)[2] and some imidazole nucleosides (e.g., **3a** → **4a**).[3] In the course of our investigation of the photolysis of *N*-(2,3-*O*-isopropylidene-α-D-ribofuranosyl)-1-amino-2-cyanocyclohexene (**3a**) we observed that its UV absorption at 265 nm was rapidly bleached when it was irradiated with a 254-nm light source in methanol solution.[3] This enamino nitrile absorption gradually returned when the bleached solution was allowed to stand in the dark for 60 h. The elucidation of the structure and mechanism of formation of this bleached product is the subject of this report.



1 2

a, R = H; b, R = CH_3; c, R = $PhCH_2$; d, R = $(CH_3)_3C$

Initially we assumed that bleaching involved an intramolecular reaction between the 5′-hydroxyl group on the ribose moiety and the excited state of the enamino nitrile chromophore[4] because this bleaching phenomenon had not been detected previously when **1a**, **1b**, **1d**, or other enamino nitriles were irradiated in methanol solution. An intramo-

(1) Ferris, J. P.; Orgel, L. E. *J. Am. Chem. Soc.* **1966**, *23*, 1974. Sanchez, R. A.; Ferris, J. P.; Orgel, L. E. *J. Mol. Biol.* **1967**, *30*, 223–53. For recent discussion see: Ferris, J. P.; Joshi, P. C.; Edelson, E. H.; Lawless, J. G. *J. Mol. Evol.* **1978**, *11*, 293–311.

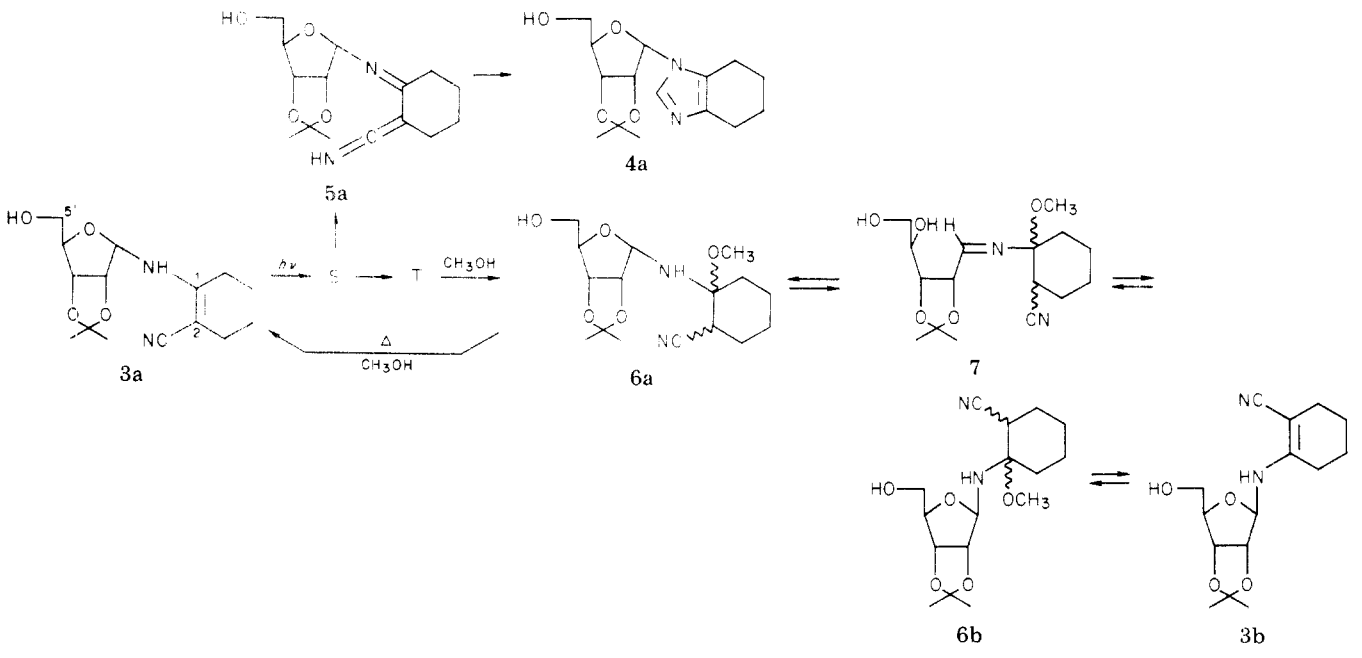
(2) Ferris, J. P.; Trimmer, R. W. *J. Org. Chem.* **1976**, *41*, 19–24. Ferris, J. P.; Narang, R. S.; Newton, T. A.; Rao, V. R. *Ibid.* **1979**, 44, 1273–1278.

(3) Ferris, J. P.; Rao, V. R.; Newton, T. A. *J. Org. Chem.*, preceeding paper in this issue.

(4) Fourrey, J.-L.; Jouin, P. *Tetrahedron Lett.* **1977**, 3397–400.

0022-3263/79/1944-4381$01.00/0

Scheme I



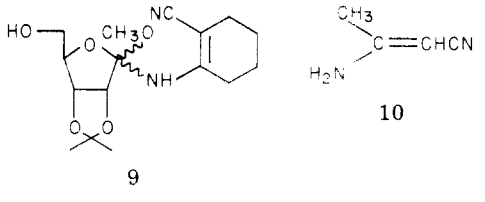
lecular reaction was shown to be unlikely by the observation that both the α anomer (**3a**) and β anomer (**3b**) undergo the photobleaching and thermal regeneration of the enamino nitrile chromophore at the same rates (see Scheme I). The rates of the intramolecular cyclization of the ribose 5′-hydroxy group and the enamino nitrile grouping in **3a** and **3b** would be expected to differ dramatically.

Our observation of the bleaching of **3** prompted us to reexamine the photolysis of simple cyclic enamino nitriles, and indeed, we were able to detect the bleaching of **1** in methanol. Photobleaching was not detected previously with simpler enamino nitriles[2] because of the more efficient rearrangement of **1** to **2** and the rapid reversion of the bleached products formed from **1** to the starting enamino nitriles. Consequently, the steady-state concentration of bleached products formed from enamino nitriles such as **1** is low.

It was possible to perform spectral studies on the bleached product formed from **3a** before it reverted back to the enamino nitrile. A crude preparation was obtained for spectral studies by evaporating the methanol solvent at room temperature after photolysis was complete. This preparation was shown to contain at least 70% bleached product by the observation that 70% of the UV absorption of the starting enamino nitrile at 265 nm was regenerated when the photolysate was allowed to stand at room temperature for 60 h. The IR spectrum of the photolysate exhibited sharply diminished absorption at 2210 and 1610 cm^{-1} consistent with the migration or loss of the enamino nitrile double bond. Both of these IR bands increase in intensity when a $CHCl_3$ solution of **6** is allowed to stand at room temperature overnight. The ^1H NMR spectrum of **6** exhibits four overlapping singlets at about δ 3.2. This multiplet was shown to be characteristic of the bleached product by the observation that it decreases in intensity when the solution of **6** stands at room temperature while signals characteristic of **3a** and **3b** form in its place. In addition a singlet with the same chemical shift as methanol (δ 3.4) also forms when the $CDCl_3$ solution of the photolysate is allowed to stand at room temperature.

The bleached product is assigned structure **6** on the basis of the ^1H NMR spectrum. The overlapping ^1H NMR singlets near δ 3.2 are assigned to the methoxyl groups of the isomers of **6**. Compound **6** would be expected to be isomeric at C-1 and C-2 due to the nonstereospecific addition of methanol to the enamino nitrile function. The recovery of both the α and β anomers of **3** from the bleached product formed from **3a** indicates that compound **6** is an isomeric at C-1′. Thermal loss of methanol from **6** results in the regeneration of the UV chromophore of the enamino nitrile and the observation of a singlet in the ^1H NMR due to the methanol eliminated. There was no ^1H NMR signal due to the methoxyl group of a methyl vinyl ether, a likely elimination product if the methoxyl group was attached to C-2 instead of C-1 in the bleached product.[5] The absence of the signals at δ 3.2 when the bleached product is prepared in CD_3OD is consistent with the bleached product being a methanol addition product of **3**.

The recovery of both **3a** and **3b** from the bleached product formed by irradiating **3a** requires a reaction at C-1′. The absence of a well-defined ^1H NMR signal in the δ 5.3–6 region for H-1′ led us to initially consider the 1′-*O*-methoxy derivative **9** as the structure of the bleached



product. Structure **9** was eliminated by our failure to observe hydrogen–deuterium exchange at H-1′ in the recovered enamino nitriles when the photolysis was performed in CH_3OD. Furthermore, if **9** were the structure of the bleached product, it would have been formed by proton or hydrogen abstraction from C-1′. If this were part of the mechanism for methanol addition, then it would be expected that the *N*-benzyl enamino nitrile **1c** would also undergo a facile photobleaching reaction. This was not observed; the extent of the photobleaching of **1c** was comparable to that of **1a** and **1b** and less than that of **3a**.

(5) Middleton, W. J.; Engelhardt, V. A. *J. Am. Chem. Soc.* **1958**, *80*, 2788–94. Middleton, W. J.; Little, E. L.; Coffman, D. D.; Engelhardt, V. A. *Ibid.* **1958**, *80*, 2795–806.

Although structure **6** is consistent with the bulk of the spectral data for the bleached product, the pathway for the anomerization of **3a** to **3b** remained to be established. Anomer **3b** is not formed by the direct photoisomerization of **3a** as shown by the absence of **3b** in the photolysate after the partial photoconversion of **3a** to **6**. The isomerism at C-1′ must be due to the anomerization of **6a** to **6b** during the 12-h time period required for the photolysis of **3a** to **6a**. Similar anomerizations have been reported in which the equilibrium between the α and β anomers is attained in less than 1 h.[6] Compound **7** may be formed as a transient intermediate in the interconversion of **6a** to **6b**. Appreciable concentrations of **7** are not present in the photolysate as shown by the absence of a ^{1}H NMR signal in the δ 7.5–9 region for the hydrogen of the imine function.[7] Furthermore, the bleached product was not reduced with sodium borohydride, a reaction characteristic of imines.[8]

The apparent absence of a signal for H-1′ in the bleached product remained to be explained. Our initial failure to detect this signal was due in part to its diffuse nature because of the presence of isomers of **6**. In addition, the signal for H-1′ overlaps with the signals from some of the other ribose ring protons. This overlap is apparent if the δ 5.15 region is monitored during the course of the conversion of **6** to **3**. The decrease in the broad ^{1}H NMR signal at δ 5.15 parallels the increase in the signals for H-1′ in **3a** and **3b**.

It was established previously that the photochemical cyclization of enamino nitriles proceeds from the singlet excited state while the cis–trans isomerism of the enamino nitrile double bond proceeds from the triplet excited state.[2,9] This was shown by the observation that the cis–trans isomerization of enamino nitriles is sensitized by benzophenone and triphenylene and is quenched with piperylene. The cyclization of the enamino nitriles to imidazoles is not sensitized by these triplet sensitizers.[9] These findings were confirmed in the present study when it was observed that the conversion of **3a** to imidazole **4a** in acetonitrile solution was not sensitized by benzophenone and was not quenched by piperylene.

The formation of the bleached product **6** was shown to proceed from the triplet excited state by sensitization experiments. Irradiation of a methanol solution of **3a** and triphenylene with a 350-nm light source resulted in the formation of **6** as shown by the characteristic pattern of four singlets at δ 3.2 in the ^{1}H NMR. No bleaching was observed when triphenylene was omitted from the reaction mixture. Since energy transfer from triphenylene to enamino nitriles had been established previously,[9] these findings establish that the bleached product is formed from the triplet excited state.

Acid or base catalysis of the methanol addition was eliminated by appropriate control reactions. The possibility that methoxide ion, generated by a basic excited state of **3a**, added to the enamino nitrile was eliminated by the absence of bleaching of **3a** with sodium methoxide in methanol. The absence of acid catalysis was established by the observation of approximately the same rate of bleaching and regeneration of the 265-nm chromophore of **3a** when the photolysis was performed in (1) methanol, (2) 10^{-2} M triethylamine in methanol, or (3) 10^{-3} M formic acid in methanol.[10,11]

The mechanism of the photobleaching reaction remained to be determined. Initially we considered the iminoketenimine **5a** to be the precursor to the bleached product **6**. Previously we observed IR bands in the 2000-cm^{-1} region, which were attributed to the ketenimine function, when enamino nitriles were irradiated at −196 °C.[2] Direct irradiation of **3a** at −196 °C as a KBr pellet also resulted in the formation of an IR band at 2030 cm^{-1} which disappeared immediately on warming. If the iminoketenimine **5a** were the intermediate in the formation of **6a**, it must have been generated via the triplet excited state of **3a**. Attempted sensitized formation of iminoketenimine **5a** was unsuccessful. Irradiation of mixtures of triphenylene or benzophenone in neat **1d**[12] cooled with liquid nitrogen did not result in the generation of an IR absorption band in the 2000-cm^{-1} region.[2]

Since our failure to observe the sensitized formation of the iminoketenimine from **1d** may be due to inefficient energy transfer due to the absence of diffusion in an alcohol matrix at −196 °C, we investigated the photochemical bleaching of **3a** and **1d** and −196 °C. A regular decrease in the UV absorption at 265 nm was observed when 10^{-4} M **1d** and **3a** were irradiated in ethanol:methanol (4:1) glasses at −196 °C. Approximately half the original UV absorption at 265 nm due to the enamino nitriles was slowly regenerated when the glasses were allowed to warm to room temperature and to stand for 24 h. In a separate experiment it was observed that the IR absorption assigned to the ketenimine function at 2030 cm^{-1} was still detectable when **1d** was irradiated in a 4:1 ethanol:methanol glass at −196 °C.[13]

The rate of loss of the ketenimine IR absorption on warming is much faster than the regeneration of the enamino nitrile UV absorption (10 min vs. 24 h, respectively). This rate difference demonstrates that the ketenimine is not the precursor to the regenerated enamino nitrile in these low-temperature photolyses. Therefore, the photobleaching observed at these low temperatures is not due to the extensive photoconversion of the enamino nitrile to the ketenimine. Furthermore, the observation of both the bleaching reaction and the IR absorption due to the ketenimine in the ethanol:methanol glass eliminated the possibility that an iminoketenimine (e.g., **5a**) is an intermediate in the formation of the bleached product.

Since the triplet states of cycloalkenes undergo alcohol addition reactions to give ethers,[11,14] we investigated this mechanistic route for the formation of the alcohol adducts of the enamino nitriles. The Markovnikov addition of alcohols to simple cycloalkenes was shown to proceed from a strained transoid triplet state since no alcohol adducts were formed from acyclic olefins.[14] The transoid triplet states of cycloalkenes would be expected to be strained because of the constraint of the ring system. We tested the possibility that a strained triplet was the reaction intermediate by irradiating at 10^{-4} M solution of acyclic β-aminocrotononitrile **10** in methanol. There was a decrease in the UV absorption for **10** at 257 nm and an in-

(6) Cusack, N. J.; Hildick, B. J.; Robinson, D. H.; Rugg, P. W.; Shaw, G. *J. Chem. Soc., Perkin Trans. 1* **1973**, 1720–31. Cusack, N. J.; Robinson, D. H.; Rugg, P. W; Shaw, G.; Lofthouse, R. *J. Chem. Soc., Perkin Trans. 1* **1974**, 73–81.

(7) King, J. F.; Durst, T. *Can. J. Chem.* **1962**, *40*, 882–889.

(8) Billman, J. H.; Diesing, A. C. *J. Org. Chem.* **1957**, *22*, 1068–70. Begland, R. W.; Hartter, D. R.; Jones, F. N.; Sam, D. J.; Sheppard, W. A.; Webster, O. W.; Weigert, F. J. *Ibid.* **1974**, *39*, 2341–50.

(9) Ferris, J. P ; Kuder, J. E. *J. Am. Chem. Soc.* **1970**, *92*, 2527–33.

(10) Cristol, S. J.; Lee, G. A.; Noreen, A. L. *Tetrahedron Lett.* **1971**, 4175–8.

(11) Kropp, P. J.; Reardon, E. J., Jr.; Garbel, Z. L. F.; Willard, K. F.; Hattaway, J. H., Jr. *J. Am. Chem. Soc.* **1973**, *95*, 7058–67.

(12) Compound **1d** was used for this experiment because it is a liquid at room temperature. This makes it easier to dissolve the sensitizer in the neat **1d** and then freeze the mixture to a glass.

(13) This experiment could not be performed with **3a** because it was not sufficiently soluble in 4:1 ethanol:methanol for IR measurements.

(14) Marshall, J. A. *Acc. Chem. Res.* **1969**, *28* 33–40. Marshall, J. A. *Science* **1970**, *170*, 137–41. Kropp, P. J. *Mol. Photochem.* **1978**, *9*, 39–65.

crease in the absorption at shorter wavelengths due to the formation of 4-methylimidazole. Little increase in absorbance at 257 nm was observed when the photolysate was allowed to stand at room temperature for over 60 h. The absence of regeneration of the β-aminocrotonitrile (**10**) chromophore coupled with the previous observation of only 4-methylimidazole as a photoproduct in methanol and ethanol established the absence of the alcohol addition reaction. The occurrence of photobleaching with the cyclohexene enamino nitriles **1** and **3** and its absence with the acyclic enamino nitrile **10** is consistent with the transoid triplets of **1** and **3** as the intermediates resulting in the Markovnikov addition of alcohols. A triplet mechanism is consistent with our observation that both the methanol addition reaction of the cyclic enamino nitriles and the cis–trans isomerism of the acyclic enamino nitrile **10** proceed when triplet sensitizers are used.[9]

Since the ketenimine can be detected under conditions when the alcohol addition reaction takes place (4:1 ethanol:methanol, −196 °C), it must be formed from the excited singlet state of the enamino nitrile. Because the photochemical rearrangement of enamino nitriles to imidazoles proceeds from the excited singlet state, these data provide further support to our hypothesis[2] that an iminoketenimine intermediate (e.g., **5a**) is the initial enamino nitrile photoproduct. This iminoketenimine undergoes a thermal cyclization and rearrangement reaction at room temperature to give the corresponding imidazole.

Experimental Section[15]

1-(*N*-Benzylamino)-2-cyanocyclohexene (1c). A mixture of 2-oxocyclohexanecarbonitrile (1.23 g, 10 mmol),[16] benzylamine (1.07 g, 10 mmol), and acetic acid (0.25 mL) was heated at reflux in 5 mL of benzene for 1 h. The reaction mixture was washed with 5 mL each of 1 N NaOH, water, and saturated salt solution, dried over sodium sulfate, and concentrated to dryness to give a 95% yield of the title compound. A sample was purified by crystallization from benzene–petroleum ether: mp 86–87 °C; UV max (CH_3OH) 209 nm (ε 5180), 278 (11 850); IR ($CHCl_3$) 3450, 2930, 2180, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.56 (m, 4, 2 CH_2), 2.16 (m, 4, 2 CH_2), 4.31 (d, 2, J = 6 Hz, CH_2), 4.95 (b, 1, NH), 7.30 (s, 5, 5 CH); mass spectrum (70 eV), m/e 211 (M − 1).

Anal. Calcd for $C_{14}H_{16}N_2$: C, 79.21; H, 7.60; N, 13.20. Found: C, 78.97; H, 7.41; N, 13.06.

Irradiation of 1 and 10 in Methanol Solution. (a) Irradiation of a degassed 10^{-4} M methanol solution of **1a** with a 254-nm light source for 8 min resulted in a decrease in the absorbance at 265 nm from 1.64 to 0.34. The solution was allowed to stand at room temperature for 19 h, and the absorbance at 265 nm increased to 0.9.

(b) Irradiation of a 10^{-4} M solution of **1c** under the same conditions as those for **1a** for 3 min resulted in a decrease in the absorbance at 278 nm from 1.63 to 0.52. The absorbance at 278 nm increased to 0.88 when the photolysate was allowed to stand at room temperature for 19 h. The imidazole corresponding to **1c** was provisionally identified as one of the photoproducts after 3 h of irradiation of a 2.3×10^{-3} M solution. The photolysate exhibited a ^1H NMR signal at δ 7.8 characteristic of H-2 of the imidazole.

(c) Irradiation of a 10^{-4} M solution of **1d** under the same conditions as those for **1a** for 3.5 h resulted in a decrease in the absorbance at 279 nm from 1.64 to 0.26. The absorbance at 279 nm increased to a constant value of 0.4 after the solution stood in the dark for 1 h.

(d) A commercial sample of β-aminocrotonitrile (**10**) was purified by recrystallization from benzene followed by sublimination (mp 74–78 °C). A 10^{-4} M solution was degassed and irradiated. The absorbance at 257 nm decreased from 1.94 to 0.44, and the absorbance in the 220-nm region increased over a 60-min time period. The absorption at 257 nm increased from 0.44 to 0.50 when the photolysate was allowed to stand at room temperature for 3 h. No further increase was noted over the next 60 h.

Irradiation of 3a and 3b in Methanol. (a) When 3 mL of a 10^{-4} M solution of **3a**[3] in methanol was degassed and irradiated for 4 min, the absorbance decreased from 1.52 to 0.10. The absorbance increased to a constant value of 1.14 when the photolysate was allowed to stand in the dark for 60 h. The same extent of bleaching and the same rate of recovery of the enamino nitrile in the dark reaction was observed when **3b** was the starting material as was observed with **3a** as the starting material. No bleaching was observed when the photolysis of **3a** was performed on an acetonitrile solution. The formation of **4a** in acetonitrile was detected by the increase in absorbance at 230 nm.

(b) In experiments designed to test if the methanol addition reaction was sensitive to the pH of the reaction medium, 10^{-4} M solutions of **3a** were prepared in the following solvents with methanol that had been distilled from Na_2CO_3: (1) methanol, (2) 10^{-2} M triethylamine in methanol, (3) 10^{-3} M formic acid in methanol. The solutions were degassed and irradiated for 4 min to bleach the absorbance at 265 nm. The 265-nm chromophore was regenerated at about the same rate and extent in each solution when the solutions were then allowed to stand at room temperature for 88 h. The pH of each reaction solution was determined with moistened pH Hydrion paper before and after photolysis. The acidity remained constant (±0.1) at the following pH values: (1) 5.3, (2) 6.2, (3) 4.1.

Irradiation of 3a in Ethanol and 2-Propanol. When 100 mg of **3a** was irradiated in 60 mL of either alcohol for 17 h, it was converted exclusively to **4a** as shown by UV and ^1H NMR. When 3 mL of a more dilute (10^{-4} M) solution of **3a** was degassed and irradiated for 2 min, the absorption at 265 nm decreased from 1.76 to 0.58. After 24 h the absorption increased to a constant value of 0.92.

***N*-(2,3-*O*-Isopropylidene-D-ribofuranosyl)-1-amino-1-methoxy-2-cyanocyclohexane (6).** (a) Irradiation of 100 mL of a 10^{-3} M solution of **3a** in methanol for 19 h and evaporation to dryness gave a product mixture of 30% **4a** and 70% **6**. The ^1H NMR spectrum ($CDCl_3$) exhibited a multiplet centered at about δ 3.2 which disappeared on standing overnight while a singlet at δ 3.4 appeared in its place. The IR spectrum ($CHCl_3$) exhibited very weak bands at 2210 and 1610 cm^{-1} which increased in intensity on standing overnight.

(b) The reaction was repeated by irradiating 200 mg of the title compound in 60 mL of CH_3OD for 13 h with a 254-nm light source. The mixture was allowed to stand at room temperature for 96 h, and the solvent was removed by evaporation. The residue was dissolved in $CDCl_3$, and compounds **3b** (84 mg), **3a** (40 mg), and **4a** (40 mg) were separated by preparative TLC using 9:1 $CHCl_3$:CH_3OH. The absence of an NMR signal at δ 7–8 for the methine proton of the imidazole ring of **4a** indicates that hydrogen–deuterium exchange of the N–H proton of **3a** took place prior to photocyclization. Neither **3a** nor **3b** contained deuterium at H-1′ as shown by the presence of NMR signals characteristic of these protons. The reaction was repeated with 75 mg of **3a** dissolved in 3 mL of CD_3OD and an irradiation time of 14 h. The bleached product did not exhibit a multiplet at δ 3.2 in the NMR. Peaks characteristic of the β anomer **3b** were observed when the solution was allowed to stand at room temperature overnight.

(c) A solution of 100 mg of **3a** in 100 mL of methanol was degassed and irradiated for 2 h. The methanol was evaporated, and the ^1H NMR spectrum of the photolysate was monitored at different time intervals. Initially only the presence of **3a**, **4a**, and **6** were apparent with no trace of **3b**. After 24 h the signals due to the bleached product disappeared, and those of **3b** appeared in their place.

Photosensitized Addition of Methanol to *N*-(2,3-*O*-Isopropylidene-2-α-D-ribofuranosyl)-1-amino-2-cyanocyclohexene (3a). A saturated solution of triphenylene (~115 mg)[17] was prepared in 100 mL of methanol, and 50 mg of the title compound was added to it. The mixture was degassed and irra-

(15) For general experimental procedures see ref 3. The samples were irradiated in quartz vessels in a Rayonet reactor equipped with lamps with principal emission at 254 nm unless otherwise noted.

(16) von Auwers, K.; Bahr, T.; Frese, T. *Justus Liebigs Ann. Chem.* **1925**, *441*, 68–100.

(17) Triphenylene from Aldrich Chemical Co. was recrystallized from benzene–petroleum ether; mp 196 °C.

diated with a 350-nm light source in a Pyrex vessel for 48 h. The photolysate was concentrated to 5 mL, the precipitated triphenylene was filtered, and the filtrate was concentrated to dryness. The NMR of the residue exhibited a multiplet at δ 3.2 and signals at δ 5.28 and 6.3 characteristic of **3b**. When the same experiment was repeated with 100 mg of triphenylene in 100 mL of acetonitrile, the NMR spectrum of the product was identical with that of the starting **3a**. A similar experiment in which 40 mg of benzophenone and 60 mg of **3a** in 100 mL of acetonitrile were irradiated for 40 h by using a 350-nm light source and a Pyrex vessel led only to the recovery of **3a**. No photolysis was observed when 50 mg of **3a** was irradiated at 350 nm for 50 h in a Pyrex vessel in 100 mL of methanol in the absence of the sensitizer.

Attempted Quenching of the Photochemical Conversion of 3a to 4a. Solutions of **3a** (10^{-4} M) in acetonitrile were irradiated with a 254-nm light source in the presence of piperylene in the concentration range 4×10^{-4}–2×10^{-3} M. The conversion of **3a** to **4a** was not inhibited.

Attempted Reaction of 3a with $NaOCH_3$. (a) A saturated solution of $NaOCH_3$ in CH_3OH which contained 10^{-4} M **3a** was monitored by UV for 20 h. There was no change in the absorption spectrum.

(b) A solution of 10 mg of **3a** in 10 mL of CH_3OD saturated with CH_3ONa was stirred at room temperature for 1 h. The ^1H NMR obtained on evaporating the solution to dryness indicated that both α and β anomers (**3a** and **3b**) were present but that H-1′ was not exchanged with deuterium.

Attempted Reduction of Photobleached Product (6) with $NaBH_4$. A solution of 100 mg (0.33 mmol) of **3a** in 60 mL of CH_3OH was degassed and irradiated at 254 nm for 7.5 h. The solvent was removed by evaporation, and the oily residue was dissolved in 5 mL of ethanol and was stirred with 15 mg (0.4 mmol) of $NaBH_4$ overnight. The solvent was distilled, and the oily residue was dissolved in $CHCl_3$, washed with water, dried, and concentrated to an oil. The NMR spectrum of the oil exhibited NMR signals characteristic of both **3a** and **3b**.

Low-Temperature Photolyses. Samples were cooled with liquid nitrogen and irradiated through quartz windows in the apparatus of Richtol and Klappmeier.[2,18] An IR band was detectable at 2030 cm^{-1} on irradiation of **3a** with a 254-nm source for 1 h in a KBr matrix. Irradiation of glasses, prepared by cooling a neat sample of **1d** or a solution of it in 4:1 ethanol:methanol, with a 254-nm light source for 1 h also resulted in the formation of an infrared band at 2030 cm^{-1}. In all the above experiments the absorption at 2030 cm^{-1} disappeared within 10 min after evaporation of the liquid nitrogen. Mixtures of triphenylene and **1d** or benzophenone and **1d**, in which the IR absorption bands of the sensitizer were roughly equal in intensity to that of **1d**, were cooled with liquid nitrogen and irradiated with a 350-nm light source. No new IR bands were detectable after irradiation. Irradiation of 10^{-4} M **3a** or **1d** in 4:1 ethanol:methanol, after cooling with liquid nitrogen, with a 254-nm source for 1–2 h resulted in the loss of the absorption of the enamino nitriles. Their absorption maxima were partially regenerated after the mixture was warmed to room temperature and maintained there for 24 h.

Acknowledgment. We thank P. Dudgeon for performing some of the experiments and G. Brooks for technical assistance. This work was supported by Grant No. CA-14511 from the National Cancer Institute, a Project Seed Grant from the American Chemical Society to G. Brooks, and NASA Grant No. NGR 33-018-148 for the support of P. Dudgeon.

Registry No. **1a**, 15595-71-8; **1c**, 71734-94-6; **1d**, 57090-86-5; **2c**, 26751-12-2; **3a**, 71734-86-6; **3b**, 71734-87-7; **4a**, 71734-88-8; **6a**, 71734-95-7; **6b**, 71734-96-8; **10**, 1118-61-2; 2-oxocyclohexanecarbonitrile, 4513-77-3; benzylamine, 100-46-9.

(18) Richtol, H. H.; Klappmeier, F. H. *J. Chem. Phys.* **1966**, *44*, 1519–23. Richtol, H. H.; Klappmeier, F. H. *Appl. Spectrosc.* **1964**, *18*, 113.

Bromination of Cytosine Derivatives

H. Taguchi[1] and S. Y. Wang*

Program in Environmental Chemistry, Department of Environmental Health Sciences, The Johns Hopkins University, School of Hygiene and Public Health, Baltimore, Maryland 21205

Received November 2, 1978

The reactions of cytosine (**6a**), 5-bromocytosine (**8a**), cytidine (**6b**), 5-bromocytidine (**8b**), 1-methylcytosine (**18a**), 5-bromo-1-methylcytosine (**8c**), 1,N^4-dimethylcytosine (**18b**), 5-bromo-1,N^4-dimethylcytosine (**18c**), 5-bromo-1,3-dimethylcytosine (**38**), 5-methylcytosine (**39**), N^4,5-dimethylcytosine (**40**), and 1,4,4-trimethylcytosine (**41**) with bromine or *N*-bromosuccinimide in aqueous or methanolic solutions have been studied. Product analyses and UV spectral changes observed at different pHs strongly support an addition–elimination mechanism. This is further substantiated by the synthesis and characterization of the previously unavailable bromohydrin intermediates, 5-bromo-6-hydroxy-5,6-dihydro and the corresponding -6-methoxy derivatives of **6a**, **8a**, **6b**, **8b**, **8c**, **18a**, **18b**, **18c**, **38**, **39**, **40**, and **41**. The final products of bromination were 5-bromocytosine (**8**) or 5-bromouracil (**3**) derivatives. The former resulted from direct dehydration of the bromohydrins and the latter from deamination prior to dehydration. From the UV spectra of these new 5,6-dihydrocytosine compounds and the related cyclobutyl dimers and bisulfite adducts, a scheme for calculation of the UV absorption maxima of hydrocytosine derivatives was deduced. The empirical values for bathochromic shifts due to substituents distinct and characteristic for amino (λ_{max} 239 nm, ϵ ~10 000) and imino (λ_{max} 227 nm, ϵ ~5000) forms are given.

On the basis of experimental data, the following sequence of reactions for the bromination of uracil (Ura) derivatives (**1**) was first suggested.[2] This mechanism was subsequently confirmed and extended.[3] The first step in the sequence resulted in the formation of the unstable bromohydrin derivatives (**2**) which were subsequently converted to the 5-bromouracil (BrUra) derivatives (**3**), probably by spontaneous or acid-catalyzed dehydration. In the presence of an excess of Br_2 or HOBr, however, the prod-

(1) Kyoto Women's University, Division of Natural Sciences, Kyoto, 605, Japan.

(2) S. Y. Wang, *Nature (London)*, **180**, 91 (1957); *J. Org. Chem.*, **24**, 11 (1959).

(3) A. M. Moore and S. M. Anderson, *Can. J. Chem.*, **37**, 590 (1959); see also D. J. Brown, "The Pyrimidines", Interscience, New York, 1962, p 174.

0022-3263/79/1944-4385$01.00/0