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PHOTODECARBOXYLATION AND PHOTOHYDRATION OF PYRIMIDINE DERIVATIVES[1]

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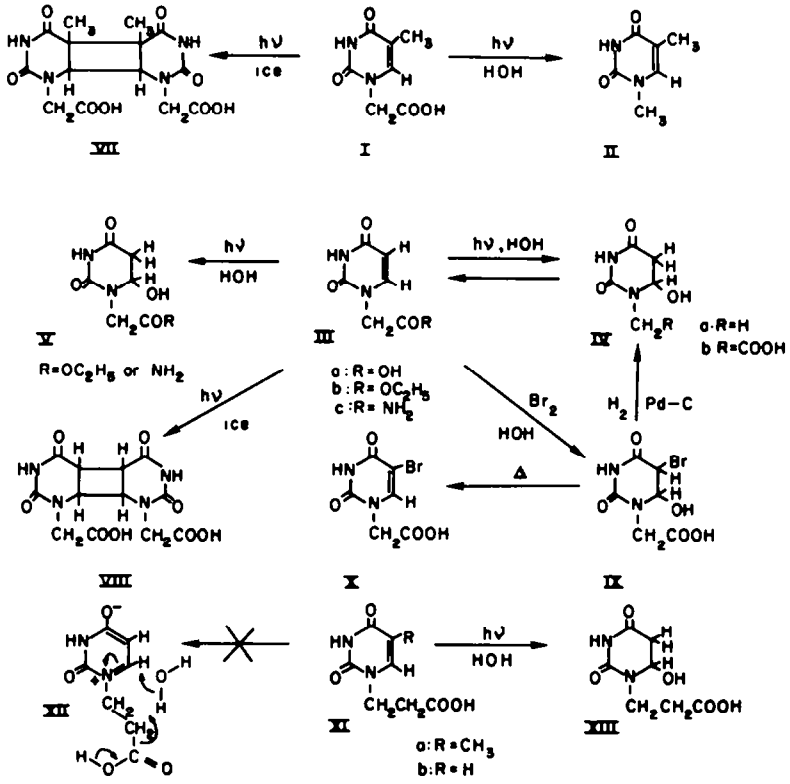
Abstract –Thymine-1-acetic acid is shown to undergo photodecarboxylation while uracil-1-acetic acid is subject to photohydration and photodecarboxylation. In contrast, no photodecarboxylation was observed for thymine-1-propionic acid and uracil-1-propionic acid. With the esters and amides of these acids, only photohydration occurred. In no instance was lactonization or azalactone formation detected in these photoreactions. Irradiation of these compounds in the dry solid state resulted in little change; however, in frozen aqueous solutions cyclobutyl dimers were isolated without decarboxylation. Detailed mechanistic study revealed that photohydration and photodecarboxylation of these pyrimidines probably are simultaneous processes which may occur from the vibrationally excited levels of the ground state.

INTRODUCTION

THE photohydration of uracil and its derivatives has been extensively studied.[4] Prolonged irradiation of uracil derivatives and their photohydrates, e.g., 1,3-dimethyl-6-hydroxy-5,6-dihydrouracil, results in the formation of N,N′-dimethylmalonamide.[5] Thymine derivatives, like uracils, probably undergo photohydration since prolonged irradiation of 1,3-dimethylthymine in aqueous solution results in N,N′-dimethylmethylmalonamide.[6] Inability to isolate the intermediate thymine photohydrates was attributed to their instability since they may readily revert to starting materials.[6, 7] It seemed reasonable to suppose that these photohydrates could be stabilized by lactonization if suitable N_1-substituents were employed. Consequently, thymine-1-acetic acid (I) and uracil-1-acetic acid (IIIa) were prepared and irradiated in aqueous solutions. Instead of the expected lactonization, compound I converted to 1-methylthymine (II) by quantitative decarboxylation, while IIIa gave 1-methyl-6-hydroxy-5,6-dihydrouracil (IVa) through hydration and decarboxylation (Scheme 1). These results prompted an investigation to determine whether the processes of hydration and decarboxylation are interrelated or whether each depends separately on photic energy absorption, since both I and IIIa undergo hydration.

It is understandable that photohydration cannot occur in compounds irradiated as dry solid films, but photodecarboxylation[8] and photolactonization[9] have been observed under such reaction conditions. Photodimerization, too, can occur in solid state in compounds having crystalline structure arrangements favorable for such intermolecular processes.[10] However, when I and IIIa were irradiated as dry solid films, no detectable evidence of any photochemical change was observed, and the original compounds were recovered These results indicate that absorption of photic energy alone is not responsible for decarboxylation, and that lactone formation is unlikely in these reactions. The improbability of lactone formation was also indicated by the fact that the corresponding photohydration products (Table 1) were quanti-



SCHEME I

tatively isolated from aqueous solutions of uracil-1-ethylacetate (IIIb) and uracil-1-acetamide (IIIc). In no instance was the formation of lactone or azalactone detected.

In frozen aqueous solutions pyrimidines presumably undergo photodimerization from singlet state, although some dimerization proceeds via triplet state in solution.[11] Irradiation of I and IIIa in ice resulted in the formation of the expected cyclobutyl dimers VII and VIII as the major products, with no loss of carbon dioxide. Decarboxylation could conceivably occur after photodimerization or photochemical saturation of the 5,6-double bond, as a simple thermal reaction.

Ground state decarboxylation after saturation of the 5,6-double bond was then tested. Heating of the bromohydrin (IX), which was obtained by the addition of one mole equivalent of Br_2 to IIIa,[12] gave 5-bromouracil-1-acetic acid (X). Hydrogenolysis of IX yielded the unstable water addition product IVb[12] which, after being allowed to stand, was isolated as IIIa. Thus, the presence of the 6-OH group in the saturated molecules does not facilitate decarboxylation in both cases. Thermally, decarboxylation of (I) and (IIIa) was observed only at temperatures of $> 280°C$ in Pyrex tubes. These results suggest that ground state decarboxylation after photohydration is unlikely for these compounds.

In view of the above results, it is reasonable to consider the possibility that photohydration and photodecarboxylation are interrelated. Since it has been shown that in acetonitrile-water mixtures photohydration rates vary directly as the square of water concentration[13, 14] it seemed that this solvent system could be used to test whether hydration and decarboxylation are interdependent. When (IIIa) was irradiated in

acetonitrile-water mixtures, the amount of decarboxylation product (IVa) formed was found to be directly related to the percentage of reaction proceeding *via* hydration. Thus, theoretically, decarboxylation should occur either immediately after or simultaneously with hydration. If decarboxylation should precede the hydration step, 1-methyluracil would be an intermediate and would have identical rates of hydration with (IIIa). However, the hydration rate of a 0·1 mM aqueous solution of (IIIa) at 32° was $64{\cdot}4 \times 10^{-3}$ min^{-1} and was 30% faster than that of 1-methyluracil ($51{\cdot}3 \times 10^{-3}$/min^{-1})[15] indicating that decarboxylation does not occur before hydration. Decarboxylation probably does not occur as a result of absorption of photic energy by hydration product because when a solution of (IVb) was subjected to irradiation, only (IIIa) was detected.

It is probable that hydration and decarboxylation are concerted simultaneous processes. If one assumes that a certain electronic configuration stabilizes a carbanion or free radical intermediate, then decarboxylation must precede hydration. This, however, is inconsistent with the above observations. Likewise, conceivable concerted ionic processes would suggest that thymine-1-propionic acid (XIa) and uracil-1-propionic acid (XIb) should decarboxylate as do I and IIIa. But, XIa was isolated without change and XIb was converted to 6-hydroxy-5,6-dihydrouracil-1-propionic acid (XIII) without decarboxylation.

It is interesting to note that when an additional $-CH_2$-group is present, decarboxylation no longer occurs. Similar effects are well known in ground state decarboxylation of carboxylic acids and are due to unfavorable electronic configuration.[16] It is conceivable that additional modes of vibrational energy relaxation provided by the extra $-CH_2$-group could prevent decarboxylation of the propionic acids (XIa and XIb). On the other hand, if decarboxylation is the result of electronic energy transfer from the pyrimidine ring to the carboxyl group, both the acetic and the propionic acids might undergo decarboxylation.[17]

Our results seem to suggest that both the decarboxylation and hydration processes may occur from the same intermediate species. Since hydration proceeds via singlet state mechanisms, this intermediate species might be either the lowest lying singlet or a species derived from it. Two suggestions have been made regarding this intermediate species: (1) that it might be a vibrationally excited species;[15] or (2) that it might be another singlet species resulting from protonation of the initial singlet species.[13] In either case, our results indicate that these species are derived from the initial singlet excited state and must possess energy of at least 40 Kcal/mole. If the former suggestion is substantiated and these reactions do in fact have rate-limiting steps involving species other than electronically excited singlet and triplet states, they may provide a clear example of the role of vibrationally excited states in solution photochemistry, especially in cases like this in which solvent molecules serve as a reactant. If it is assumed that the intermediate species have energies of about 50 Kcal/mole and are vibrationally excited, reaction from these vibrationally excited levels may be more likely, considering the very large energy difference between them and the lowest lying singlet state, the energy of which is about 90 Kcal/mole.[19]

EXPERIMENTAL

Irradiation apparatus. This was described in a previous report.[12] G. E. Germicidal lamps (G 15T8; mainly 254 nm) were used as the light source.

TABLE 1. MOLECULAR FORMULAS, M.PS AND ELEMENTAL ANALYSES OF SUBSTITUTED PYRIMIDINES AND THEIR PHOTOPRODUCTS

Compound	Formula	m.p.[a] (°C)	% Calc C	% Calc H	% Calc N	% Found C	% Found H	% Found N
1-Methylthymine	$C_6H_8N_2O_2$	255–257 (dec)	51·42	5·72	20·00	51·66	5·96	20·04
1-Methyluracil	$C_5H_6N_2O_2$	235–236	47·62	4·76	22·22	47·44	4·45	22·22
1-Methyl-6-hydroxy-5,6-dihydrouracil	$C_5H_8N_2O_3$	156–157	41·66	5·59	19·44	41·56	5·63	19·25
Ethyl Uracil-1-acetate	$C_8H_{10}N_2O_4$	152	48·48	5·05	14·14	48·55	5·00	14·10
Ethyl-6-hydroxy-5,6-dihydrouracil-1-acetate	$C_8H_{12}N_2O_5$	137–138	44·44	5·59	12·96	44·40	5·57	13·37
6-Hydroxy-5,6-dihydrouracil-1-acetamide	$C_6H_8N_3O_3$	180 (dec)	38·50	4·81	22·45	38·20	4·99	22·50
Uracil-1-acetic acid cyclobutyl-dimer	$C_{12}H_{12}N_4O_8$	dec > 280	42·35	3·53	16·47	42·58	3·50	16·31
Thymine-1-acetic acid cyclobutyl-dimer	$C_{14}H_{16}N_4O_8$	dec > 280	45·65	4·75	15·21	45·85	4·43	15·00
5-Bromouracil-1-acetic acid	$C_6H_5N_2O_4Br$	dec > 280	28·93	2·02	11·24	29·20	2·15	10·85
Thymine-1-propionic acid	$C_8H_{10}N_2O_4$	174–175	48·48	5·05	14·14	48·56	5·15	14·28

[a] Uncorrected as determined on Fisher Johns melting point apparatus

TABLE 2. UV SPECTRA OF N^1-SUBSTITUTED PYRIMIDINES

Compound	λ_{max} (nm)			$\varepsilon_{max} \times 10^{-3}$			λ_{min} (nm)			$\varepsilon_{min} \times 10^{-3}$		
	HCl[a]	HOH	NaOH[b]	HCl[a]	HOH	NaOH[b]	HCl[a]	HOH	NaOH[b]	HCl[a]	HOH	NaOH[b]
1-Methylthymine	268	268	266	7·40	7·40	5·55	234	234	244	1·30	1·30	2·55
Thymine-1-acetic acid	265	270	268	9·60	9·80	7·67	232	235	244	2·17	2·27	5·15
Uracil-1-acetic acid	260	264	263	9·80	10·3	7·62	228	232	240	1·53	1·81	4·27
1-Methyluracil	267	267	—	9·15	9·15	—	238	238	—	1·30	1·30	—
Ethyl Uracil-1-acetate	260	260	263	11·3	11·3	10·0	228	228	240	2·80	2·80	6·00
Uracil-1-acetamide	264	265	262	10·5	10·4	7·00	230	230	240	1·80	1·50	4·40
5-Bromouracil-1-acetic acid	278	281	278	8·40	8·20	6·10	240	241	250	1·40	1·40	2·80

[a] Measured in 0·1N HCl
[b] Measured in 0·01N NaOH

TABLE 3. PHOTOPRODUCTS COMPOSITIONS OF URACIL-1-ACETIC ACID IN ACETONITRILE AND WATER MIXTURES

Composition of mixture (Acetonitrile–Water)	Per cent hydration (±1%)	Per cent 1-MU formed (±4%)
100–0	0	0
75 25	20	18
50–50	36	34
25·75	62	58
0–100	98	97

Paper chromatography. Samples were applied on Whatman No. 1 or No. 3 paper (for isolation study) and were developed in the following solvent systems by descending technique:

(A) n-butanol and water (86:14); (B) n-butanol, water and conc. NH_4OH (86:14:1); (C) 95% ethanol and 1 M ammonium acetate pH 7·5 (70:30); (D) isopropanol, water and conc NH_4OH (70:20:10); (E) n-propanol, water and conc NH_4OH (70:20:10); (F) n-propanol and water (70:30).

After elution, UV absorbing spots were located with a viewer and their respective amounts were quantitatively estimated by UV absorbancy after elution. To detect the presence of cyclobutyl dimers, the chromatograms were cut into 1 in. bands; each was eluted with 10 ml water: and their spectra were determined before and after irradiation.

Column chromatography. Samples were applied on a 6 × 80 cm Dowex 50-X8 (H^+, 100–200 mesh) column. Distilled water was used as the eluent and fractions of 25 ml of the eluent were collected. These fractions were combined to form large fractions according to the UV spectroscopic evidence for isolation study.

Thymine-1-acetic acid (I). The method of Smith and Binkly[20] was used to prepare thymine-1-acetic acid. The m.ps and elemental analyses of compounds synthesized and photoproducts isolated are listed in Table 1; their UV spectra are listed in Table 2.

Irradiation of thymine-1-acetic acid (I) *and the isolation of 1-methylthymine* (II). A 1 mM aqueous soln of I (3 l.) with initial pH of 3·2 was irradiated for 1 hr at 32°. This resulted in an 8% irreversible spectral decrease and the pH of the soln was increased to 5·0. The irradiated soln was freeze-dried and the residue was collected. It weighed 390 mg when dry. Portions (20 mg) of this material were chromatographed on paper for separation and detection of photoproducts. The information so obtained was used for isolation study. The R_f values are given below.

Eluent	R_f Value I	1-Methylthymine (II)
A	0·00	0·48
B	0·00	0·47
C	0·64	0·82

To isolate the photoproduct, 180 mg of the crude material was applied on paper and was developed with eluent A. The absorbing band with R_f of 0·48 was cut out and extracted thoroughly with abs MeOH. After evaporation, the residue weighed 162 mg. Recrystallization from abs MeOH gave material which melts at 255–257° with dec.

Identical results were obtained when I was irradiated in pH 7 buffered soln.

Uracil-1-acetic acid (IIIa). The method of preparation was analogous to that for I. IIIa was obtained in a yield of 85%, m.p. 293° with dec (Lit. 295).[21]

Irradiation of uracil-1-acetic acid (IIIa) *and the isolation of 1-methyl-6-hydroxy-5,6-dihydrouracil* (IVa). A 1 mM aqueous soln of IIIa (3 l.) with initial pH of 3 1 was irradiated for 2 hr at 32°. This resulted in an increase in pH to 5 and in a 90% decrease in absorbancy which was reversible with heat and acid. The soln was frozen immediately after irradiation and was lyophilized. The dried material weighed 390 mg. The UV spectrum of this material showed that little dehydration occurred during this operation.

Photoproducts formed and their percentages were determined by paper chromatography. The results are given below.

Eluent	R_f	Percentage	Compound
A	0·05	3	IIIa
	0·37	45	1-MU
	0·46*	52	IVa
B	0·06	6	IIIa
	0·48	94	1-MU
	—	-	—
C	0·59	6	IIIa
	0·64	52	1-MU
	0·80*	42	IVa

* Band visible only after exposing to steam and Conc HCl vapor.

Portions (100 mg) of the lyophilized material were dissolved in 2 ml of distilled water, applied on paper, and developed with eluent A. The band with R_f value of 0·37 of the chromatogram was cut out and the material was thoroughly extracted with abs MeOH. Upon concentration, crystalline material with m.p. 235–236° was obtained.

Portions (100 mg) of the lyophilized material were dissolved in 5 ml of abs EtOH, then mixed with 100 mg charcoal and filtered. This was concentrated to 1 ml at room temp and 10 ml light petroleum was added. After this had been allowed to stand, crystalline product with m.p. 156–157° was obtained. A total of 75 mg recrystallized material was collected. The compound possessed little absorbancy > 240 nm but its spectra became identical to that of 1-methyluracil upon heating in acid pHs. Its IR in KBr pellet showed an OH band at 2·98 μ.

Identical results were obtained with IIIa irradiated in pH 7 phosphate buffered solutions

Irradiation of thymine-1-acetic acid (I) *and uracil-1-acetic acid* (IIIa) *as thin solid films.* Each 5 ml portion of 1 mM aqueous soln of I or IIIa was gradually applied to a glass plate and dried with a drier to an even film. It was then desiccated overnight. Films of I and IIIa were irradiated for 1 and 2 hr, respectively. After irradiation, the plates were rinsed several times with 0·5 ml distilled water; the extracts were combined and adjusted to a volume of 5 ml. As a control, plates containing films of unirradiated I and IIIa were similarly treated. No difference was observed between the UV spectra (1/10 dilution) of the irradiated and unirradiated samples. For IR spectra determination the contents of 5 plates of irradiated and 5 plates of unirradiated samples were eluted with 10 ml distilled water. They were evaporated until dry, desiccated, ground with 75 mg KBr, and made into pellet. Again, no detectable difference was observed in the IR spectra of the irradiated and unirradiated I and IIIa. Chromatography in solvent systems A, B, and C again confirmed that the only compounds detected were I and IIIa for irradiated and unirradiated samples.

Preparation of ethyl uracil-1-acetate (IIIb). A catalytic amount of conc H_2SO_4 (0·2 ml) was added to a suspension of 1·0 g uracil-1-acetic acid in 40 ml abs EtOH. After refluxing for 90 min, the mixture became a clear soln. After 4 hr the refluxing was stopped and most of the excess EtOH was then removed. The remainder was taken up in 50 ml chloroform. The hot chloroform soln was filtered twice through 1 g $NaHCO_3$ to remove both the H_2SO_4 and the unreacted material. After each filtration, the funnel was washed with hot chloroform. The combined filtrate and washings were evaporated until dry. The white residue, wt 1·0 g, melted at 152°.

Irradiation of ethyl uracil-1-acetate (IIIb) *and the isolation of ethyl 6-hydroxy-5,6-dihydrouracil-1-acetate* (Va). A–1 mM aqueous soln of IIIb (3 l.) was irradiated for 2 hr at 32° causing a 90% heat-reversible UV spectral change. This reversibility indicated that photohydration was the main reaction. The irradiated soln was freeze-dried and the residue was extracted 3 times with 7 ml of abs EtOH. After removing the EtOH at room temp, the thoroughly dried material weighed 630 mg. Portions (30 mg) of this material were chromatographed on paper for separation and quantitation of the photoproduct. The R_f values are given below

Eluent	R_f Value IIIb	Va*
A	0·83	0·64
C	0·75	0·75
F	0·85	0·85

* Detected after exposing chromatograms to steam and conc HCl fume.

The photoproduct was isolated in a yield of 80% by the same charcoal method used for IVa; the crystals melted at 137–138°. The UV spectrum of the product showed very little UV absorbancy at > 240 nm; its IR spectra in KBr pellet showed an intense OH band at 2·80 μ.

Identical results were obtained with IIIb irradiated in pH 7 buffered solns.

Uracil-1-acetamide (IIIc). The method of preparation was that of McElvain and Tate.[22] The m.p. was 288–290°.

Irradiation of uracil-1-acetamide (IIIc) *and the isolation of 6-hydroxy-5,6-dihydrouracil-1-acetamide* (Vb). A 1 mM aqueous soln of IIIc (2 l.) was irradiated for 1 hr, causing a 95% heat-reversible UV spectral change. After freeze-drying and extracting, 326 mg residue was recovered. Paper chromatography was carried out for separation and quantitation of the photoproduct. The R_f values are given below.

Eluent	R_f Value IIIc	Vb*
A	0·20 (0·20)†	0·10 (0·03)
C	0·58 (0·76)	0·53 (0·64)

* Fluorescent spot

† R_f values for ascending technique

Since only one photoproduct was detected, the charcoal filtration method (same as for IVa) was again used. The product decomposed above 180° and showed very little UV absorbancy > 240 nm.

Irradiation of uracil-1-acetic acid (IIIa) *in frozen solution and the isolation of its cyclobutyl dimer* (VIII). A 1 mM aqueous soln (2 l.) was irradiated in a frozen state for 90 min at an intensity of $2·5 \times 10^3$ ergs/mm²/sec. After the irradiated soln had thawed, its spectrum was determined with appropriate dilution. A 15% spectral decrease, observed in the 260 nm region, was irreversible with heat, acid, or base treatment. However, on re-irradiation of the thawed solution for 3 min, 80% of the spectral decrease was reconstituted. This readily indicated that a cyclobutyl type dimer was the main photoproduct. The thawed soln was evaporated at room temp until dry. The residue was separated first by paper chromatography using eluent D. On the chromatograms, two bands could be detected. The one with R_f 0·21 appeared as a dark band. The other (R_f 0·06) was located as a dark spot when a thin strip was irradiated for 1 or 2 min.

Each of the bands was cut out and completely extracted with water. After concentration, they were chromatographed separately on columns. From the 0·21 band, 250 mg were recovered in fractions 9–11. This compound was shown by UV, IR and mmp to be the unreacted starting material. From the 0·06 band, three compounds were separated. In fractions 17–20, 3 mg of a 310 nm absorbing product were isolated.[23] In fractions 9–11, 10 mg of the starting material were recovered. In fractions 5–8, 15 mg of a photoproduct were obtained; it decomposed at temperatures above 280°.

Irradiation of thymine-1-acetic acid (I) *in frozen solution and the isolation of its cyclobutyl dimer* (VII). When a method identical to that described above for IIIa was used, a 20% spectral decrease resulted. This decrease was not reversible by treatment with acid, base or heat but 70% of the absorbancy was restored when the thawed soln was re-irradiated for 3 min. The residue from the irradiated soln was separated into two bands on paper chromatograms developed with eluent D. When the material from the R_f 0·31 band was re-chromatographed on a column, it gave 198 mg of the starting compound collected in fractions 11–13. The material from the R_f 0·05 band was separated into 3 compounds on column chromatography. About

20 mg of unreacted I was recovered in fractions 11 13. Small amounts of 310 nm absorbing material were observed in fractions 19 34. The dimer VII collected from fractions 7 10 amounted to 45 mg. VII reconverted quantitively to I when it was irradiated for 1 min in aqueous soln. VII melted above 280° with dec.

Preparation of 5-bromouracil-1-acetic acid (X).[12] Compound IIIa (2 g) was pulverized and suspended in 100 ml water. Br_2 (0·7 ml, 1·2 mol eq) was added and the mixture was stirred, with a clear soln resulting. The soln was then heated on a steam bath for 1 hr during which period a ppt gradually accumulated. After cooling, the product (2·6 g) was collected and melted at 275 280° (dec). After repeated recrystallization from hot water, it melted at 280° with dec.

Preparation of 6-hydroxy-5,6-dihydrouracil-1-acetic acid (IVb). To 0·51 g of IIIa suspended in 20 ml distilled water, 0·17 ml Br_2 was added. When, after swirling for about 5 min, the soln became clear, 4 ml of pH 7 phosphate buffer was added. Spectral determinations before and after the addition of buffer showed little UV absorption at > 230 nm. Catalytic hydrogenation at 5° was carried out with the addition of 0·2 g 10% Pd C, about 93% of the theoretical amount of H_2 was taken up in 35 min The reaction mixture was then filtered through a Celite pad and was applied on a column in a cold room. IVb was obtained in about 20% yield from fractions 2 and 3. However, after being permitted to stand at room temp, it converted to IIIa, as determined by UV spectra and m.p.

Irradiation of 6-hydroxy-5,6-dihydrouracil-1-acetic acid (IVb). IVb was prepared according to the procedure described. After Celite filtration, the filtrate containing IVb was diluted 10 to 100 with distilled water (5°) and was irradiated for 30 min at 15–18°. After irradiation, the product in the soln was dehydrated by boiling for 30 min. It was then concentrated, applied on paper and developed, as described for the irradiation of IIIa. The results clearly showed that no 1-MU was present; only IIIa was found, indicating that decarboxylation did not occur with IVb upon irradiation.

Irradiation of uracil-1-acetic acid (IIIa) *in acetonitrile–water mixtures.* Solutions of IIIa (0·5 mM) in acetonitrile water mixtures of varying proportions (see Table 3) were irradiated until a 50–80% spectral decrease resulted. Portions of this irradiated soln were used for the following determinations

Spectral reconstitution. A 10 ml aliquot was introduced into a 10 ml volumetric flask and was heated in a boiling water bath for 1 hr, during which interval the acetonitrile evaporated. After cooling and readjusting the volume to 10 ml, 2·5 ml of the soln was diluted to 10 ml for UV spectra. As a control, 10 ml of the unirradiated sample was treated in an identical manner.

Quantitation of 1-MU. After reconstitution, the soln was concentrated, quantitatively applied on paper and chromatographed with eluent F. The band with R_f 0·64 due to 1-MU was eluted with 40 ml water and its UV spectra determined. On the basis of ε_{max} 9150, the amount of 1-MU was estimated. In addition to the starting material (R_f 0·20), two other products with R_f 0·42 and 0·55 were detected from the irradiated samples, the amounts of these products decreased as the percent of hydration product increased. An unirradiated sample treated in the same manner showed only the band of IIIa.

Preparation of thymine-1-propionic acid (XIa). Acrylonitrile (4·8 ml) was added to 50 ml of 1N KOH containing 2 g thymine and the mixture was refluxed. The evolution of ammonia, which indicated the beginning of the reaction, was monitored with litmus paper. After 4 hr, the evolution of ammonia had ceased and heating was stopped. After cooling, the soln was washed 3 times with 30 ml chloroform and twice with ether. The aqueous soln was then concentrated to about 25 ml and acidified to pH 2. The crystalline product was separated by refrigeration. Another portion was recovered by evaporating the filtrate until dry, and the residue was extracted 3 times with 20 ml acetone water (9 : 1). This product was combined further and purified by titrating with sat $KHCO_3$ aq until no more effervescence was observed. Undissolved material was removed by filtration. The filtrate was then acidified to pH 2 by the dropwise addition of conc HCl. The resulting ppt was collected and recrystallized from hot water. A total of 2·5 g of XIa was obtained and melted at 174 175°

Irradiation of thymine-1-propionic acid (XIa) *in aqueous solution.* A 1 mM aqueous soln of XIa (1 l.) was irradiated for 1 hr at 32°, causing about 3% irreversible spectral decrease in the 270 nm. No photoproduct could be detected by chromatography, spectral reversibility or characteristic reactions. Over 95% of the material was recovered as unreacted XIa. Under identical conditions, I quantitatively decarboxylated to 1-methylthymine.

Preparation of uracil-1-propionic acid (XIb). The method of preparation was the same as for XIa. A total of 2·45 g purified material was obtained, m.p. 185–186° (Lit. 185–186°).[24]

Irradiation of uracil-1-propionic acid (XIb) *in aqueous solution.* A 1 mM aqueous soln of XIb (3 l.) was irradiated for 90 min under conditions like those described for IIIa. This resulted in the complete disappearance of UV absorbancy at the 260 nm region, 95% of which was reconstituted by acid, base or heat.

Various attempts to isolate this photohydrate of XIb were unsuccessful. Its presence was demonstrated in the following manner. The irradiated soln (1 l.) was filtered through charcoal in order to remove all substances having UV absorption. This filtrate, which had no UV absorption > 240, was freeze-dried. The residue, 120 mg, was hygroscopic and again showed no UV absorption > 240 nm when dissolved. On heating, it was quantitatively reconverted to XIb.

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