investigative groups, and the fact that these same two groups both found glycine and alanine in the free state in hot water extracts of the Apollo 11 samples (*10, 11*).

A third sample of Apollo 11 fines was extracted three times with hot water, and the extracts were subjected to hydrolysis and analysis. The results are presented in Fig. 2. These results demonstrate that the first extraction was complete and that no contamination was introduced into the sample during processing in this laboratory. The ability to detect more amino acids, by types and amounts, might, however, result from further improvement in the methods. The small amounts of amino acids found and the fact that the proportions in the trench sample are the lowest examined suggest that the amino acid precursors may be products of the reaction of components of the solar wind (*18*), or from passage of the solar system through clouds of interstellar matter. Such an inference deserves to be tested by analysis of other subsurface samples.

The amino acids released by the method described are mainly similar to those reported for the Murchison meteorite (*15*). Although some reservations apply in each case and although the history of the meteorite poses especially difficult questions, the results from both sources may be viewed as supporting each other and providing evidence for the existence of extraterrestrial amino acids. The results are consistent with firmer data on the convertibility of components of interstellar matter to amino acids (*7*) and on laboratory models constructed under geologically relevant conditions (*2*).

KAORU HARADA
Institute of Molecular Evolution and Department of Chemistry, University of Miami, Coral Gables, Florida 33134
P. E. HARE
Geophysical Laboratory, Carnegie Institution, Washington, D.C. 20008
C. R. WINDSOR, S. W. FOX
Institute of Molecular Evolution and Department of Biochemistry, University of Miami

References and Notes

1. Other possible sources of extraterrestrial organic matter are a number of carbonaceous chondrites. These, however, all have a history of travel through the earth's atmosphere, in which they could have accumulated organic matter, for example, pollen grains as shown for the Orgueil meteorite [F. W. Fitch and E. Anders, *Ann. N.Y. Acad. Sci.* **108**, 495 (1963)], of repose on the earth's surface [during which bacterial infection of the interior of the meteorite can occur rapidly; A. A. Imshenetsky, in *Life Sciences and Space Research*, A. H. Brown and M. Florkin, Eds. (Spartan Books, Washington, D.C., 1966), vol. 4, p. 60], and a history of a period of high temperature at the anterior surface which can wreak chemical changes to yield products that can be driven into the interior. The general possibility of contamination due to the handling of meteorites has also been pointed out by those who have examined the Murchison meteorite (*15*).
2. S. W. Fox, *Nature* **205**, 328 (1965); *Naturwissenschaften* **56**, 1 (1969); ———, K. Harada, G. Krampitz, G. Mueller, *Chem. Eng. News* **48**, 80 (22 June 1970).
3. G. Mueller and G. W. Hinsch, *Nature* **228**, 254 (1970).
4. S. W. Fox, K. Harada, P. E. Hare, G. Hinsch, G. Mueller, *Science* **167**, 767 (1970).
5. A. C. Cheung, D. M. Rank, C. H. Townes, D. D. Thornton, W. J. Welch, *Phys. Rev. Lett.* **21**, 1701 (1968); L. E. Snyder, D. Buhl, B. Zuckerman, P. Palmer, *ibid.* **22**, 679 (1969); L. E. Snyder and D. Buhl, *Astrophys. J.* **163**, L47 (1971).
6. K. Harada, *Nature* **214**, 479 (1967).
7. S. W. Fox and C. R. Windsor, *Science* **170**, 984 (1970).
8. P. E. Hare, in *Organic Geochemistry*, G. Eglinton and M. T. J. Murphy, Eds. (Springer-Verlag, New York, 1969), p. 438.
9. S. W. Fox and J. F. Foster, *Introduction to Protein Chemistry* (Wiley, New York, 1957).
10. B. Nagy, C. M. Drew, P. B. Hamilton, V. E. Modzeleski, M. E. Murphy, W. M. Scott, H. C. Urey, M. Young, *Science* **167**, 770 (1970).
11. P. E. Hare, K. Harada, S. W. Fox, in *Proceedings of the Apollo 11 Lunar Science Conference*, A. A. Levinson, Ed. (Pergamon, New York, 1970), vol. 2, p. 1799; analyses of samples from Apollo 11 (sample 10086) and from Apollo 12 (trench sample 12033 and surface sample 12001) were reported in the symposium on the Origin of Life, Paleobiogeochemistry at the meeting of the International Association for Geochemistry and Cosmochemistry, Tokyo, 8 September 1970, by S. W. Fox, P. E. Hare, K. Harada, and C. R. Windsor.
12. B. Nagy, C. M. Drew, P. B. Hamilton, J. E. Modzeleski, V. E. Modzeleski, L. A. Nagy, W. M. Scott, J. E. Thomas, H. C. Urey, R. Ward, paper presented at the Apollo Lunar Science Conference II, Houston, 12 January 1971.
13. C. Ponnamperuma *et al.*, *Science* **167**, 760 (1970).
14. J. Oro *et al.*, *ibid.*, p. 765.
15. K. Kvenvolden, J. Lawless, K. Pering, E. Peterson, J. Flores, C. Ponnamperuma, I. R. Kaplan, C. Moore, *Nature* **228**, 923 (1970); K. Kvenvolden, J. Lawless, C. Ponnamperuma, *Proc. Nat. Acad. Sci. U.S.* **68**, 486 (1971).
16. B. R. Simoneit, A. L. Burlingame, D. A. Flory, I. D. Smith, *Science* **166**, 733 (1969).
17. Profiles from rinses of the skin of various humans are virtually indistinguishable.
18. S. Chang, K. Kvenvolden, J. Lawless, C. Ponnamperuma, I. R. Kaplan, *Science* **171**, 474 (1971).
19. Reprints should be requested from S. W. Fox. Work aided by NASA grant NAS 9-8101. Contribution No. 190 of the Institute of Molecular Evolution, University of Miami.

26 April 1971; revised 3 June 1971 ■

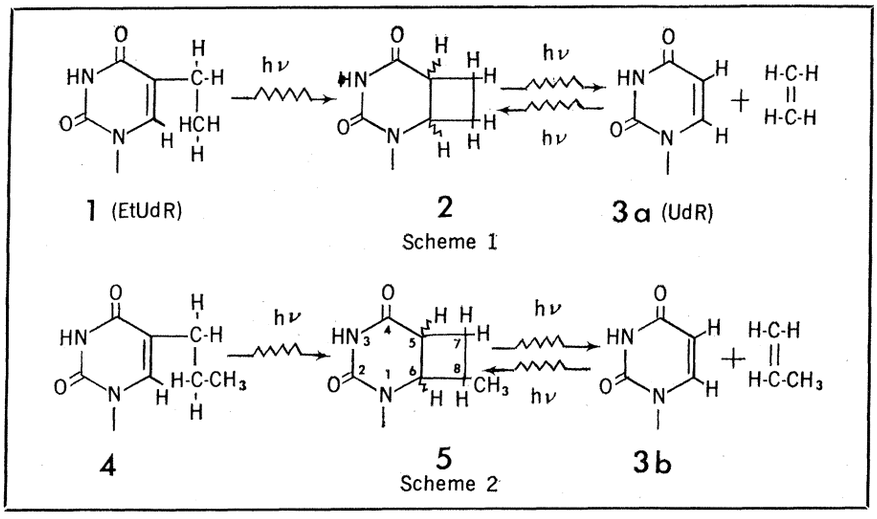
Photochemical Transformation of 5-Alkyluracils and Their Nucleosides

Abstract. *Irradiation at 254 nm of aqueous solutions of 5-ethyl-, 5-propyl-, and 5-isopropyluracils (or their nucleosides) leads to cleavage of the 5-alkyl substituents, via an intramolecular electrocyclic photoaddition intermediate, with formation of uracil (or its nucleoside). The photoaddition intermediates represent a new class of dihydropyrimidines, namely analogs of 5,6-dihydro-5,6-cyclobutanyluracil and its nucleosides; the biological significance is discussed.*

It has been demonstrated (*1, 2*) that 5-ethyldeoxyuridine (**1**, EtUdR), a nonmutagenic thymidine base analog with antiviral activity (*3*), undergoes two wavelength-dependent photochemical transformations in neutral aqueous medium. (i) At wavelengths longer than 265 nm, the principal reaction is a photodimerization, similar to that undergone by thymine or thymidine; (ii) at shorter wavelengths, 254 nm, irradiation leads to cleavage of the 5-ethyl side chain with formation of deoxyuridine (**3a**) in more than 80 percent yield (*4*). Photodimerization occurs also on irradiation at 254 nm; however, at this wavelength, the dimers exhibit absorption so that they are rapidly photodissociated and can be detected only in small quantity by paper chromatography during the initial stage of the reaction (*2*).

The behavior at 254 nm of compound **1** contrasts with that for dilute ($10^{-4}M$) aqueous solutions of **3a** and thymidine; compound **3a** undergoes mainly photohydration of the 5,6 bond; thymidine is relatively radiation resistant under these conditions (*5*). We have examined the behavior of two higher 5-alkyl analogs, 5-propyluridine (**4**) and 5-isopropyluridine, both of which were prepared on a small scale enzymatically from the corresponding bases with the aid of the uridine phosphorylase system (*6*).

Both the foregoing were only very slowly transformed to unidentified products on irradiation of 10^{-4} to $10^{-3}M$ neutral aqueous solutions at long wavelengths. But, at 254 nm, either in the presence or absence of oxygen, each readily underwent cleavage of the 5-alkyl substituent via an identifiable intermediate (**5**, see below) with formation of uridine (**3b**) in 80 to 90 percent yield. The quantum yields for these transformations were 5×10^{-3} for isopropyluridine and 9×10^{-3} for propyluridine, as compared to 21×10^{-3} for hydration of uridine. No photodimer formation was observed



with either compound, irrespective of the wavelength of irradiation, possibly because of steric hindrance by the larger 5-alkyl substituents.

Since the photochemical conversion of **1** to **3a** was shown to be accompanied by apparent liberation of ethanol, estimated by enzymatic methods (*1, 7*), we anticipated that photocleavage of the higher 5-alkyl side chains would lead to liberation of the corresponding alcohols. An examination of *freshly* irradiated solutions of 5-propyluridine and 5-isopropyluridine by gas chromatography revealed, however, that the only volatile cleavage product in both instances was propylene. Subsequent storage of the irradiated solutions led to a decrease in propylene content with the concomitant appearance of aldehydes (formic and acetic), acetone, and alcohols (ethanol, isopropanol), the aldehydes predominating in solutions irradiated in the presence of air or oxygen, and the latter in the absence of oxygen.

This prompted us to reexamine the volatile photoproducts of **1** irradiated at 254 nm. Gas chromatography immediately after irradiation now revealed only ethylene. On storage of the irradiated solution, the ethylene content decreased, with the concomitant appearance of acetaldehyde and ethanol. It follows that the ethanol previously observed by enzymatic methods (*1*) is a secondary product of the reaction of liberated ethylene with water.

It subsequently proved possible (*2*) to isolate, by thin-layer chromatography, a photointermediate of compound **1** with the spectral properties of a dihydropyrimidine (*5, 8*) which, on further irradiation at 254 nm, was quantitatively converted to uridine with a quantum yield of 0.3 and the simultaneous elimination of ethylene. The photochemical transformation of **1** to **3a** at 254 nm should therefore be represented as in scheme 1. The conversion of **1** to **2** is a typical example of an intramolecular electrocyclic photoaddition reaction (*9*); whereas the subsequent conversion of **2** to **3a**, involving dissociation of a cyclobutane ring, is formally analogous to the photodissociation of a pyrimidine photodimer.

Scheme 1 immediately suggests the possibility of photochemical addition of ethylene to **3a**. And, in fact, when **3a** was irradiated at 254 nm in the presence of ethylene (bubbled through the solution during irradiation), the major photoproduct, apart from some hydrated **3a**, exhibited spectral and chromatographic properties identical with those of **2**, and, on irradiation at 254 nm, was converted quantitatively to **3a** with the concomitant elimination of ethylene. The addition of ethylene to **3a** (scheme 1) is an example of the well-known photocycloaddition reactions of olefins to aromatic molecules (*10*).

Uridine was then irradiated on a preparative scale at a concentration of $10^{-3}M$ in neutral aqueous medium, in the presence of propylene which was bubbled continuously through the solution, in a 254 nm reactor (*11*). After 60 percent of the uridine disappeared, the irradiated solution was brought to dryness under reduced pressure at 40°C, and the residue taken up in the minimum quantity of hot water, from which, on cooling, crystallization occurred.

The photoproduct isolated in this way consisted of a mixture of crystals which, apart from differences in shape, could be distinguished under a microscope hot-stage by variations in melting points ranging from 230°–232°C to 259°–261°C, testifying to the presence of isomers. Our efforts to separate these by fractional crystallization were only partially successful, but elementary analysis of the product coincided with that expected from a 1:1 adduct of uridine and propylene. The photoproduct exhibited ultraviolet spectra in neutral and alkaline media typical of those for a 2,4-diketo-5,6-dihydropyrimidine (*5, 8*), as well as the alkaline lability characteristic for such derivatives, including reversibility of alkaline decomposition (opening of the 3,4 bond of the pyrimidine ring) by treatment with acid (*8*). Irradiation of the photoproduct at 254 nm led to elimination of propylene and quantitative regeneration of uridine with a quantum yield of 0.22. The foregoing observations are consistent with scheme 2 for the photochemical transformation of 5-propyluridine (and 5-isopropyluridine) at 254 nm.

This was further confirmed by an examination of the nuclear magnetic resonance spectrum of **5** in [$^2H_6$]dimethyl sulfoxide. One fraction (melting point at 259° to 261°C) exhibited a CH_3 doublet at 1.23 ppm due to coupling with H-8 ($J_{CH_3\text{-}H\text{-}8} = 6.8$ hz). Another fraction, with melting point at 249°–252°C, showed CH_3 signals at 1.23 ppm and 1.06 ppm with relative integral intensities of 3:1, indicating a 3:1 mixture of two isomers, of which the one present in the higher proportion is that with melting point at 259°–261°C.

The photointermediates **2** and **5**, which can be photochemically synthesized on a preparative scale, are representatives of a new class of dihydropyrimidines such as compound **2**, 5,6-dihydro-5,6-cyclobutanyluracil (or uridine or deoxyuridine), which are of potential biological significance (*12*). This new class of derivatives should also prove of value in extending our knowledge of the properties of pyrimidine photodimers, which have hitherto played a crucial role in the elucidation of genetic repair mechanisms.

ESTERA KRAJEWSKA
D. SHUGAR
Institute of Biochemistry and Biophysics, Academy of Sciences, and *Department of Biophysics, University of Warsaw, Warsaw, Poland*

References and Notes

1. I. Pietrzykowska and D. Shugar, *Science* **161**, 1248 (1968).
2. ———, *Acta Biochim. Polon.* **17**, 361 (1970).
3. M. Swierkowski and D. Shugar, *J. Med. Chem.* **12**, 583 (1969), and references cited therein.
4. The same reactions are displayed by 5-ethyluridine and by 1-methyl-5-ethyluracil, but with somewhat different quantum yields (*2*).
5. D. Shugar, in *The Nucleic Acids*, E. Chargaff and J. N. Davidson, Eds. (Academic Press, New York, 1960), vol. 3. At higher concentrations both uridine and thymidine undergo photodimerization.
6. Description of the preparation and properties of these new ribonucleosides, prepared with the aid of rat liver uridine phosphorylase (E.C. 2.4.2.3) is in preparation.
7. R. Bonischen, in *Methods of Enzymatic Analysis*, H. U. Bergmayer, Ed. (Academic Press, New York, 1963), p. 285.
8. C. Janion and D. Shugar, *Acta Biochim. Polon.* **7**, 309 (1960).
9. R. B. Woodward and R. Hoffman, *J. Am. Chem. Soc.* **87**, 395 (1965).
10. D. C. Neckers, *Mechanistic Organic Photochemistry* (Reinhold, New York, 1967).
11. M. Fikus, K. L. Wierzchowski, D. Shugar, *Photochem. Photobiol.* **4**, 521 (1965).
12. We have found that a higher alkyl analog of uridine, 5-hexyluridine, undergoes a similar reaction to yield uridine, on irradiation at 254 nm, in a yield of 50 to 60 percent (E. Sztumpf-Kulikowska and D. Shugar, in preparation). Furthermore, one can obtain the 1 : 1 photoadducts of thymidine with ethylene and propylene. These exhibit spectral and photochemical properties similar to those of the 1 : 1 adduct of uridine with propylene.

13. We thank Dr. B. Fiszer for the samples of 5-propyl- and 5-isopropyluracil used in the preparation of the corresponding nucleosides; Dr. S. Braunstein of the National Research Council of Canada, Ottawa, for the NMR spectra; and the World Health Organization, The Wellcome Trust, and the Agricultural Research Service, U.S. Department of Agriculture, for partial support of this and related investigations.

22 February 1971; revised 3 May 1971 ■

Sea Snakes: An Unusual Salt Gland under the Tongue

Abstract. *The posterior sublingual gland of sea snakes is a salt gland. It secretes a fluid surpassing seawater in sodium chloride concentration. The gland lies on the ventrolateral surfaces of the tongue sheath and empties through multiple ducts into the sheath. Fluid is expelled from the sheath when the tongue is extended. For freshly captured* Pelamis, *the plasma concentrations of sodium, chloride, and potassium were 210, 167, and 8 millimoles per liter, respectively. Injections of sodium chloride led to a rise in its concentration in the plasma and to an increase in the rate and concentration of fluid secreted by the sublingual gland. The ultrastructure of this gland is similar to that of other reptilian salt glands. However, the gland is not homologous with any other salt gland. The sublingual gland in* Pelamis *is larger than that in* Laticauda, *and the rate of electrolyte excretion from the larger gland is greater.*

Of all reptiles, only certain poisonous sea snakes have completely broken their ties with the land. Snakes such as *Pelamis*, the pelagic yellow-bellied sea snake, feed at the sea surface and bear their young at sea. These snakes are highly specialized for a marine existence, but little is known about their physiological adaptations to marine conditions.

The sea is a highly concentrated salt solution (about 470 m*M* Na, 548 m*M* Cl) with an osmotic pressure of about 1 osmolal. Most marine vertebrates, including the reptiles, maintain a body fluid concentration about one-third this amount, and they encounter problems in conserving water and excreting excess salts. The reptilian kidney, unlike kidneys of mammals and birds, cannot produce urine more concentrated than the plasma, so accessory organs known as salt glands have developed in marine forms to handle excretion of excess salts. In sea turtles and in the estuarine diamondback terrapin, the salt gland is located behind the eye and secretes "tears" into the orbit (*1*). In the marine iguana the salt gland is nasal and the secretions are sneezed out the nares (*1*). No one had previously found a salt gland in sea snakes, but Dunson had collected fluid more concentrated than seawater from the mouths of *Pelamis* and *Laticauda* (*2*).

At first the sea snake salt gland was thought to be the newly discovered *Laticauda* "natrial" gland (*3*), but we now know this is not the case because *Pelamis* does not have a natrial gland (*4*). Furthermore, the sea snake salt gland is sublingual, not nasal or orbital. Its ultrastructure generally conforms to that of other tissues specialized for electrolyte transport. The gland was cannulated and uncontaminated fluid was collected for analysis. Secretion is probably controlled by receptors for plasma salt concentration or osmotic pressure. Under natural conditions *Pelamis* maintains higher plasma salt concentrations than terrestrial reptiles do. During periods of dehydration, considerably higher plasma salt concentrations can be tolerated. Differences between sea snakes in the size, ultrastructure, and capacity for salt excretion of the salt gland seem to be related to the degree of adaptation for marine life.

Gross dissections of the lower jaw of *Pelamis* revealed an enlarged posterior sublingual gland similar in relative weight to that of known salt glands. In seven *Pelamis* averaging 63 g in body weight, the sublingual gland was 0.043 percent of the body weight compared with the heart which was 0.130 percent of the body weight. Salt glands in sea turtles, the diamondback terrapin, and the marine iguana are about 0.05 to 0.06 percent of the body weight (*5*).

The head of a small *Pelamis* was serially sectioned for examination of the anatomy of the sublingual gland, and particularly of the location of the ducts draining the gland. The head was fixed in formalin, partially skinned, and decalcified in sodium citrate (20 percent) and formic acid (2 percent). It was then dehydrated, embedded, and sectioned at 7 μm. The sections were stained with Masson's trichrome stain. The single large posterior sublingual gland covered parts of the tongue sheath almost completely. The smaller paired anterior sublingual glands lay immediately anterior to the opening of the tongue sheath. Sublabial or infralabial glands were present as were supralabial glands. A large gland, probably the Harderian, lay medial to the eye. The large venom gland was prominent posterior to the orbit (Fig. 1A). Except at the most posterior end, ducts left the posterior sublingual gland at all levels and coursed to the tongue sheath. A typical section near the middle of the gland shows three ducts joining the sheath (Fig. 1B). The sheath and the lower portion of the ducts were lined with keratinized stratified squamous epithelium. The posterior sublingual gland consisted of tubules arranged generally in a radial fashion around the central tongue sheath. At the extreme posterior end of the gland where there were no ducts, the tubules turned and ran longitudinally along the sheath. There was no indication that any other gland emptied into the tongue sheath. The anterior sublinguals emptied into the mouth by two ducts just anterior to the tongue sheath opening. Taub (*6*) reported that a rattlesnake had paired anterior sublingual glands and a single posterior sublingual gland, but in some snakes the glands were not found. In an amphibious sea snake examined in this study (*Laticauda*), the posterior sublingual gland was present, but much smaller than the gland in the pelagic *Pelamis*.