

PHOTOLYSIS OF 5-BROMO-1,3-DIMETHYLURACIL IN SUBSTITUTED BENZENES

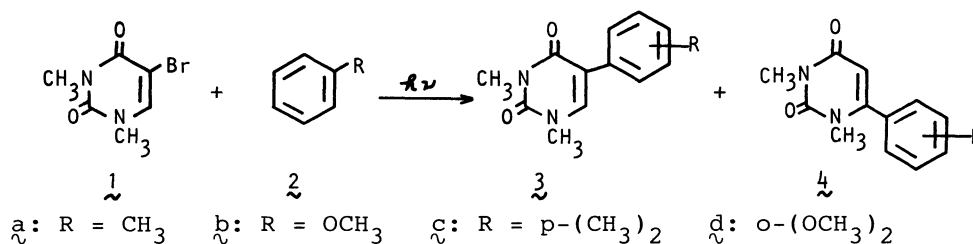
Koh-ichi SEKI,* Yuko BANDO, and Kazue OHKURA
 Faculty of Pharmaceutical Sciences, Higashi-Nippon-Gakuen
 University, Ishikari Tobetsu, Hokkaido 061-02

Photolysis of 5-bromo-1,3-dimethyluracil in toluene, xylene and anisole afforded the anomalously substituted 6-aryl-1,3-dimethyluracils beside the expected products 5-aryl-1,3-dimethyluracils, while the reaction with veratrole occurred exclusively at the 5-position of the uracil ring.

It has been well recognized that the replacement of thymine in DNA with 5-halouracil increases sensitivities of bacterial and mamalian cells to the lethal effects of ultraviolet, X-ray or γ -ray irradiation.¹⁾ Recently, attention was focused on the biological effects caused by the photo-induced cross linking between proteins and nucleic acids.²⁾ Matsuura et al.³⁾ have found that 5-bromouracil attacked photochemically at the 2-position of tryptophan derivatives to produce the coupled products in excellent yields. They further elucidated the details of the reaction mechanism.^{3,4)} However, such a regioselective attack of 5-bromouracils on indole moieties is apparently in contrast to the results observed in the photo-substitutions of indoles by halopyridines⁵⁾ or methyl chloroacetate,⁶⁾ where they attack the indole ring non-regioselectively. These results prompted us to explore the reactivities of 5-bromouracils in photoreaction. In this paper, we wish to report our findings that 6-arylluracils were produced together with expected 5-arylluracils on irradiation of 5-bromo-1,3-dimethyluracil in substituted benzenes.

A solution of 5-bromo-1,3-dimethyluracil (**1**) (200 mg) in a monosubstituted benzene (**2a, b**) (150 ml) was irradiated with a 500 W high-pressure mercury lamp in a doughnut type Pyrex vessel for 24 h under the stream of argon at room temperature. The reaction mixture was concentrated in vacuo and the residual oil was chromatographed on a Lobar column (Lichroprep RP-8, Merck) or on a silica gel column (Simpack PREP-SIL, Shimadzu) to give three regioisomers of 5-aryl-1,3-dimethyluracils (**3a, b**) and of 6-aryl-1,3-dimethyluracils (**4a, b**). The structural assignments of the products were made on the basis of their spectra (MS and ¹H NMR) and elemental analyses.

The reaction of **1** (10 mg) with disubstituted benzenes (**2c, 2d**, 10 ml) was carried out under similar conditions (reaction time, 4 h), and it was found that the 6-isomer (**4c**, R=2',5'-(CH₃)₂) was formed in a higher ratio to the 5-isomer (**3c**) in the reaction with xylene, while, in the reaction with electron rich veratrole (**2d**),⁷⁾ the substitution occurred exclusively at the 5-position of

Table 1. Formation of $\underline{3}$ and $\underline{4}$ 

$\underline{2}$	Yield of $\underline{3}/\%$ ^{a)}			Yield of $\underline{4}/\%$ ^{a)}			Ratio of $\underline{4}/\underline{3}$	Recovery of $\underline{1}/\%$ ^{a)}
	(o)	(m)	(p)	(o)	(m)	(p)		
$\underline{2a}$		19		2.8			0.15	5
	(88.5)	(6.5)	(5)	(29)	(56)	(15)		
$\underline{2b}$		21.4		3.6			0.17	6
	(65)	(23)	(12)	(27.5)	(64)	(9)		
$\underline{2c}$		45.7		12.5			0.27	20
$\underline{2d}$		15.0		0			0	67

a) Yields and isomer ratio given in parentheses were determined by isolation.

the uracil ring to afford regioisomeric 5-substituted uracils ($\underline{3d}_{2',3'}$, (R=2',3'-(OCH₃)₂) and $\underline{3d}_{3',4'}$, (R=3',4'-(OCH₃)₂) in the ratio of 47.4:52.6) with no formation of the 6-substituted derivative ($\underline{4d}$) being observed. The reaction in a benzene solution also furnished the 6-substituted product ($\underline{4e}$, R=H) beside the 5-isomer ($\underline{3e}$, R=H), but the $\underline{4e}/\underline{3e}$ ratio was fairly low (0.08). The results are summarized in the Table.

Thus, the ratio of $\underline{4}/\underline{3}$ varies with a substituent on the benzene ring, suggesting that different reaction mechanisms may be involved in the reaction. Although the reaction mechanisms participating in the reaction remain undefined, it is noteworthy that the formation of 6-substituted compounds provides the first exceptional example of photo-induced aromatic substitutions with bromouracils. Further work on the mechanisms of the present reaction is now in progress.

References

- 1) S. Y. Wang, "Photochemistry and Photobiology of Nucleic Acids," ed by S. Y. Wang, Academic Press, New York (1976), Vol. 1.
- 2) M. D. Shetlar, Photochem. Photobiol. Rev., 5, 105 (1980).
- 3) T. Matsuura, I. Saito, S. Ito, H. Sugiyama, and T. Shinmura, Pure Appl. Chem., 52, 2705, 1980, and references therein.
- 4) S. Ito, I. Saito, and T. Matsuura, J. Am. Chem. Soc., 102, 7535 (1980).
- 5) K. Seki, K. Ohkura, M. Terashima, and Y. Kanaoka, Abstract Papers, the Symposium on Photochemistry, Kanazawa, Japan, 1982, p. 33.
- 6) S. Naruto and O. Yonemitsu, Chem. Pharm. Bull., 20, 2163 (1972).
- 7) S. Ito, I. Saito, and T. Matsuura, Tetrahedron, 37, 45 (1981).

(Received November 9, 1985)