ACID-CATALYZED PHOTOREACTION OF 6-CHLORO-1,3-DIMETHYLURACIL IN BENZENE; SYNTHESIS OF CYCLOOCTAPYRIMIDINE-2,4-DIONE

Koh-ichi Seki,* Nobuhiko Kanazashi, and Kazue Ohkura

Faculty of Pharmaceutical Sciences, Higashi-Nippon-Gakuen University,
Ishikari-Tobetsu, Hokkaido 061-02, Japan

Abstract - The photolysis of 6-chloro-1,3-dimethyluracil in benzene afforded 1,3-dimethyl-6-phenyluracil, while the photoreaction in the presence of trifluoroacetic acid afforded 1,3-dimethylcyclooctapyrimidine-2.4-dione as a major product.

Since photocycloaddition of maleic anhydride to benzene was first reported,[1] there has been much work concerning the mechanistic details of the process.[2] However the synthetic application of the reaction to heterocyclic compounds has not yet been made. In our continuing studies on the photoreaction of halouracils with substituted benzenes,[3] we now report that a [2+2]cycloaddition product 1,3-dimethylcyclooctapyrimidine-2,4-dione (**1**) was first obtained by the photolysis of 6-chloro-1,3-dimethyluracil (6-ClDMU) in benzene in the presence of trifluoroacetic acid (TFA).

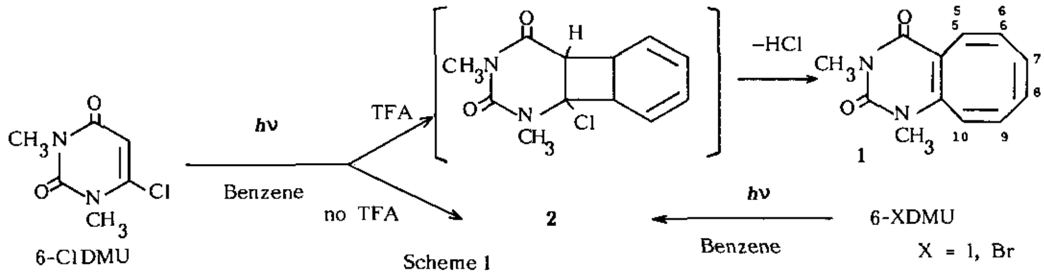
Photolysis of a solution of 6-ClDMU (4.36 mg, 0.025 mmol) in benzene (5ml) in the presence of TFA (0.05 mmol)[4] with a 500 W high pressure mercury lamp in a degassed Pyrex test tube using a merry-go-round apparatus gave **1** (mp 130-131°, yellow plates recrystallized from i-propanol)[5] in appreciable yield (62%, based on 6-ClDMU consumed), presumably led through [2+2]cycloaddition process, whereas, under the similar conditions but in the absence of TFA, 6-phenyl-1,3-dimethyluracil (**2**) was obtained in 33 % yield (Scheme 1, Table I).

The mass spectrum of **1** showed m/z 216 (100%, M^+). The proton nuclear magnetic resonance (^{1}H-nmr) spectrum of **1** (acetone-d_6) exhibited two sharp signals at 3.23 and 3.31 ppm due to the *N*-methyl groups and peaks ascribable to six vinyl protons between 5.95-6.35 ppm, which was analyzed by ^{1}H-^{1}H shift-correlated spectroscopy and nuclear Overhauser effect spectroscopy.[6]

In contrast with the above finding, photoreaction of 6-iodo- and 6-bromo-1,3-dimethyluracils (6-IDMU, 6-BrDMU) and benzene proceeded smoothly under the similar conditions to furnish **2** as a major product together with 1,3-dimethyluracil (DMU), but no **1**.[7] The added acid was inefficient on the formation of **1** or **2**, though the yield of DMU was suppressed appreciably (Table I).

No cycloadduct was obtained by the photolysis of 1,3-dimethyluracil or 1,3-dimethylthymine in benzene either in the absence or presence of TFA.

The uv spectrum of 6-ClDMU (λ_{max} 262 nm) (0.08 mM) shifted ca. 6 nm to the red in cyclohexane by the addition of TFA (9 equiv. molar).[8] This new spectrum was insensible to the added benzene, whereas the fluorescence of this solution was quenched efficiently with benzene. Furthermore, addition of a triplet quencher, piperylene, to the reaction with benzene was ineffective on the formation of **1**, suggesting that the present cycloaddition may proceed via the singlet excited state of protonated 6-ClDMU or the charge transfer complex of 6-ClDMU and TFA.



Scheme 1

Table I. Photolysis of 1,3-Dimethyl-6-halouracils (6-XDMU) in Benzene

6-XDMU/ X	Reaction time (h)	TFA (mmol)	Yields (%)[a,b] 1	2	DMU	Consumed 6-XDMU (%)[a]
Cl	10	0	—	33	—	11
	10	1.2	32	3.3	—	69
	10	0.05	62	3.8	—	41
Br	10	0	—	53	16	94
	10	0.05	—	33	8	95
I	2.5	0	—	72	1.1	71
	2.5	1.2	—	74	0.3	97

a) Determined by hplc. b) Based on 6-XDMU consumed.

It is noteworthy that the formation of **1** provides the first example of the photocycloaddition product between a uracil ring and benzene.

Further studies on the mechanisms and synthetic application of the present reaction are in progress.

REFERENCES AND NOTES

1 D. Bryce-Smith and A. Gilbert, Tetrahedron 1977, **33**, 2459.
2 J. Mattay, J. Photochem., 1987, **37**, 167, and references therein.
3 K. Seki, K. Matsuda, Y. Bando, and K. Ohkura, Chem. Pharm. Bull., 1988, **36**, 4737: K. Seki and K. Matsuda, Nucleic Acids Res., Symp. Ser., 1988, **17**, 25.
4 Similar results were obtained by using zinc chloride in place of TFA.
5 Satisfactory analytical data were obtained.
6 ^{1}H-nmr spectrum of the vinyl protons; δ (ppm)(coupling constant/Hz) H_5, 6.11(H_5-H_6, 11.49; H_5-H_7, -0.11); H_6, 5.97(H_6-H_7, 3.91; H_6-H_8, -0.34; H_6-H_9, 0.89); H_7, 6.03 (H_7-H_8, 11.58; H_7-H_9, -0.10); H_8, 6.07 (H_8-H_9, 3.21); H_9, 6.33 (H_9-H_{10}, 11.48); H_{10}, 6.22.
7 R. D. Youssefyeh and L. Lichtenberg, J. Chem. Soc. Perkin Trans. I, **1974**, 2650.
8 Similar shifts were observed for 6-BrDMU and 6-IDMU.

Received, 25th December, 1990