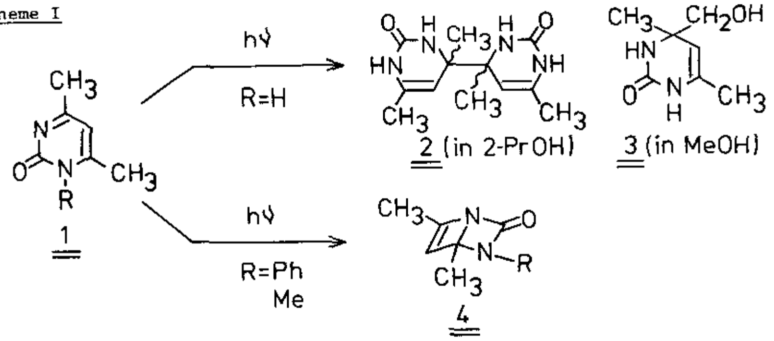
PHOTOCHEMISTRY OF CONJUGATED NITROGEN-CARBONYL SYSTEMS. 1
PHOTOADDITION OF 2-PYRIMIDONE AND SOME PROPERTIES OF THE RESULTING ENE-UREA SYSTEM[1,2]

Yuichi Kanaoka,* Masato Hasebe and Yasumaru Hatanaka
Faculty of Pharmaceutical Sciences, Hokkaido University, Sapporo 060 Japan

Photoexcited 2-pyrimidone 5 reacts with such hydrogen donors 6 as alcohol, ether and amine, to give cyclic ene-urea derivatives 7 in addition to a dimer 8. The ene-urea system 7 is fairly reactive and treatment of 7 with alcohol or thiol leads to adducts 9, 10 which are candidates as possible intermediates for enzymatic studies. Photochemical behaviors of fundamental nitrogen-carbonyl systems 11, 5, 12 are compared.

In 1975 Pfoertner reported that irradiation of 4,6-dimethyl-2-pyrimidinone 1 (R=H) in 2-propanol leads to a dihydrodimer 2, whereas in methanol an addition product 3 is formed[3] (Scheme I). As part of the systematic photochemical research on conjugated nitrogen-carbonyl systems, which stemed from our studies on photochemistry of amides and imides[4] and from our continued interests in nucleotide chemistry,[5] we have started exploring photoreactions of a variety of azabenzenes including also pyrimidones.[2] In this context, recent attention drawn to the pyrimidone system, i.e., reports on the photolyses of 1 (R=Me, Ph) to 4[6] and on that of 4-pyrimidones,[7] prompted us to communicate, in the present paper, our results that delineate general patterns of the photoaddition of 2-pyrimidone and describe some chemical properties of these photoadducts.[5]

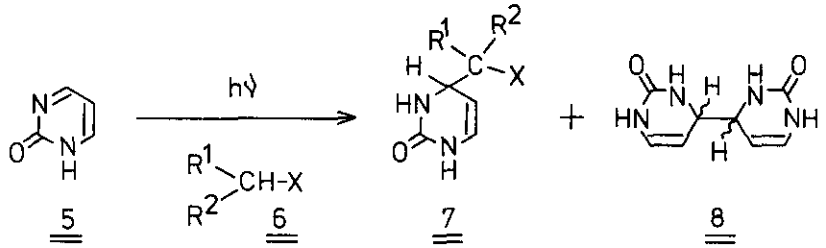
Scheme I



Irradiation of 2-pyrimidone 5 (500 mg in 450 ml of a solvent 6; 11.6 mM) led to isolation of 7 and 8 after silica-gel column chromatography as summarized in Scheme II and TABLE I.[8] In a representative example, the structural assignment for 7a was based on (i) the molecular composition $C_7H_{12}N_2O_2$ [mass m/e 156 (M^+); elemental analysis] showing a 1:1 adduct of 5 and 6a; (ii) the presence of an urea carbonyl [ir 1670 cm^{-1}] and a conjugated urea [uv, 247 nm (ε 2600), EtOH]; (iii) the presence of two methyl [^1H NMR 1.05 ppm (s)], two olefinic protons [3.68 (d), 6.05 (dd)], two

NH [6.2 (b) and 8.1 (b)] and one OH [4.44 (s)]; (iv) reasonable ^{13}C NMR [DMSO-d_6]. Assignment 8 was based on (i) the dimeric composition [mass 194 (M^+)] and (ii) other spectral data.

Scheme II



a: $R^1=R^2=$ Me, X = OH
b: $R^1=R^2=$ H, X = OH
c: $R^1=$ H, R^2- X $=-(CH_2)_3-O-$
d: $R^1=$ H, $R^2=$ Me, X $=-N-Et_2$

TABLE I Photoaddition Products from 5

Product	Reaction time	mp °C[a)]	Yield[b)]	Yield of 8[b)]
7a	11 hr	141-50(A)	27 %	32 %
7b	20	53-5(A)	30	34
7c	8	124-7(A)	72	25
7d	44	c) 83-5(EH) 149-50(E)	34 24	40

a) recrystallization solvent: A, acetone; E, ether; H, n-hexane.

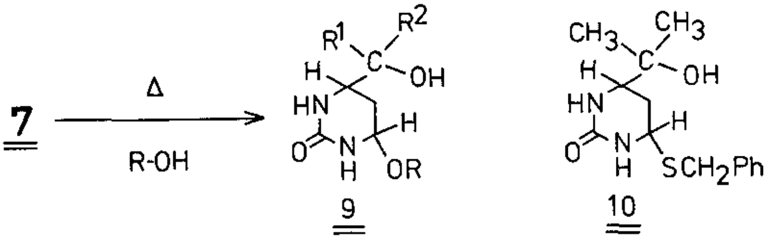
b) Elution with ($CHCl_3$: MeOH), (95:5 v/v) then (85:15 v/v), afforded 7 followed by 8 [mp 280-3° (dec)].

c) diastereoisomers separated by silica-gel chromatography using (MeOH:AcOEt = 5:95 v/v).

The results shown in TABLE I indicate that there is a unity of reactive behavior of such reagents as alcohol, ether and amine 6, with a hydrogen on carbon α to the hetero atom, toward photoexcited 2-pyrimidone. Thus on irradiation, the pyrimidone 5 generally undergoes addition reaction with a good hydrogen donor molecule such as 6, at the expense of the C=N bond to lead to cyclic ene-urea derivatives 7. A photodimerization competes as well under these reaction conditions.

Chemistry of dihydrouracil derivatives has attracted much attention. 5,6-Dihydrouracils are common photo-hydrated products of pyrimidine nucleotides,[9] as well as metabolic intermediates of thymidylate synthetase.[10] 3,4-Dihydrouracils, on the other hand, may serve as models of intermediates during the study of deaminases.[11] In view of such increasing interest in both chemistry and biochemistry of nucleotides, some chemical properties of 7 were examined. As shown in Scheme III, the ene-urea system 7 underwent facile (thermal) addition reactions to give adducts 9, which are candidates as possible intermediates in the mechanistic studies of the enzymes.[10,11] Treatment with benzylthiol gave also a similar adduct 10.

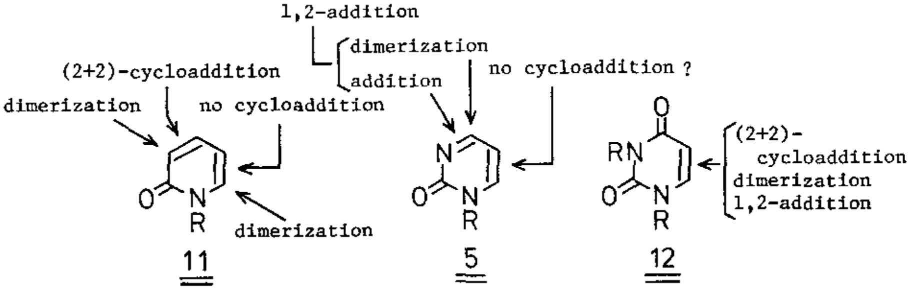
Scheme III



a: $R^1=R^2=$ Me, R = Et
b: $R^1=R^2=$ H, R = Et
c: $R^1=R^2=$ H, R = Me

In Scheme IV, photochemical behavior of a series of fundamental cyclic nitrogen-carbonyl systems, 11, 5 and 12, are compared in terms of their addition reactions. 2-Pyridone 11, the simplest member of the family, undergoes both 1,4-[12] and 1,2-additions,[13] at the C_3-C_6 sites and the C_3-C_4 double bond, respectively, while irradiation of uracils 12 mainly leads to 1,2-addition at the C_5-C_6 double bond.[9] For 2-pyrimidone 5, which comes formally between 11 and 12 with regard to the functionality, its major reaction is the 1,2-addition involving the C=N bond as described in the present work, and the reactivity of the C_5-C_6 double bond is likely unimportant. However, further study is needed for settling the latter problem. Possible reactivities of the C_5-C_6 double bond of 2-pyrimidone, for example, toward [2 + 2] cycloaddition are now under investigation.

Scheme IV Intermolecular Photoreactions of the Nitrogen-Carbonyl Systems



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