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A MULTI-STEP PHOTOREACTION OF 5-FORMYL-1,3-DIMETHYLURACIL WITH INDOLE IN THE SOLID STATE

Ji-ben Meng,[a] De-chao Fu,[a] Zhen-hen Gao,[a] Ru-ji Wang,[b] Hong-gen Wang,[b]
Isao Saito,[c] Ryuichiro Kasatani,[c] and Teruo Matsuura[c*]

[a]Department of Chemistry and [b]Central Laboratory, Nankai University, Tianjin, China
[c]Department of Synthetic Chemistry, Faculty of Engineering,
Kyoto University, Yoshida, Kyoto 606, Japan

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Abstract - Irradiation of the mixed crystals between 5-formyl-1,3-dimethyluracil (**1**) and indole (**2**) gave 5-(bis-1-indolyl)methyl-1,3-dimethyluracil (**3**), whereas 1,3-dimethyluracil was the sole product in the photolysis of **1** and **2** in solution.

A recent trend in photochemical research is directed to photochemistry of supramolecular assemblies, namely more complex systems than simple solutions.[1-4] We have made various approaches to this problem focusing photochemistry of organic molecules in the solid state.[5-13] Among these approaches, we have been particularly interested in bimolecular photoreaction between two different organic molecules in the solid state, since a relatively few attention has been made to this field.[14] For example, irradiation of the mixed crystals of indole and phenanthrene gave an adduct in the solid state but no reaction occurred in organic solvents.[7] We now describe a novel multi-step photoreaction of 5-formyl-1,3-dimethyluracil with indole occurring only in the solid state.

Mixed crystals, prepared by resolidifying the melt of a mixture of 5-formyl-1,3-dimethyl-uracil (**1**) and indole (**2**) crystals (molar ratio 1 : 3), were irradiated with a high-pressure mercury lamp for 4 hours gave a photoproduct **3** in 40 % yield. The structure of **3** was assigned as 5-(bis-1-indolyl)methyluracil on the basis of its spectral data and finally confirmed by an X-ray crystallographic analysis (Figure 1, Table 1-2). The solution photochemistry of 5-formyl-1,3-dimethyluracil (**1**) was quite different from the solid-state one. Irradiation of **1** in acetonitrile or methanol with a high-pressure mercury lamp under nitrogen gave 1,3-dimethyluracil (**4**) as the major product in the presence of indole and no formation of **3** was observed. It is of interest that **1** having a conjugated enal group underwent neither usual [2 + 2]cycloaddition nor photoreduction in solution.

Since the formation of **3** in the solid state appeared to involve a two-step photoreaction between **1** and two molecules of indoles, the time course of the reaction was examined. The result is shown in Figure 2 indicating the formation of an intermediate. However, the isolation of this intermediate was unsuccessful owing to its instability on a silica gel column. Although the structure of the intermediate remains to be elucidated, the intermediary formation of an indole oxetane **5**[15] may be plausible which will react photochemically or thermally to give **3**. The proximity effect of the substrate molecules in the mixed crystal appears to be responsible for the facile formation of **3**.

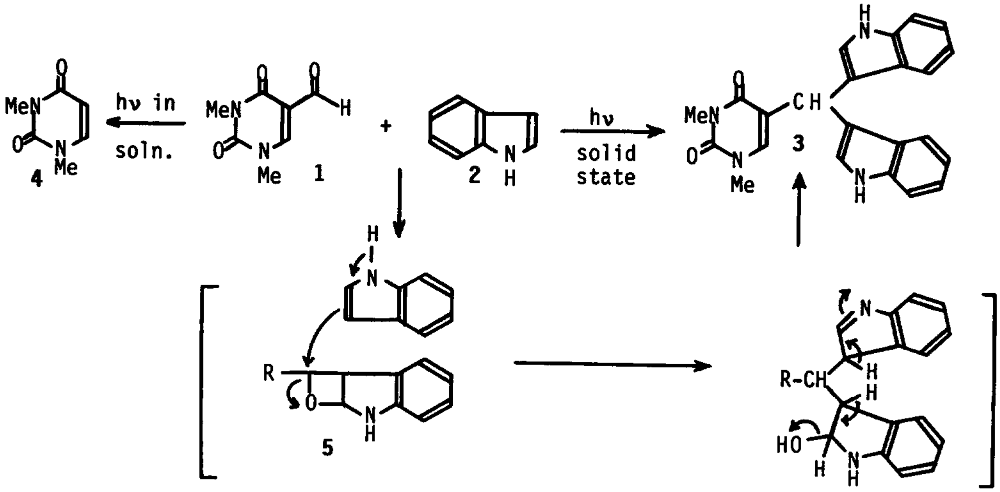

Table 1. Positional parameters for non-hydrogen atoms of 3 with estimated standard deviations in parentheses.

Atom	x	y	z	Beq.(02)
C	1.0372(4)	-0.0283(5)	0.2391(2)	3.1(1)
N11	0.9956(4)	0.0332(5)	0.1647(2)	5.1(1)
C12	0.8947(4)	-0.0389(5)	0.1155(2)	3.6(1)
N13	0.8579	0.0238(4)	0.0492(2)	3.67(9)
C14	0.9135(5)	0.1411(5)	0.0282(2)	4.0(1)
C15	1.0057(4)	0.2011(4)	0.0770(2)	2.25(9)
C16	1.0442(4)	0.1506(5)	0.1432(3)	3.5(1)
017	0.8446(3)	-0.1463(4)	0.1283(2)	5.08(9)
C18	0.7506(5)	-0.0396(6)	-0.0017(3)	5.6(1)
019	0.8795(3)	0.1849(4)	-0.0330(2)	4.91(9)
C20	1.0611(6)	0.3275(7)	0.0572(3)	5.8(2)
C22	1.1697(4)	0.0181(5)	0.2747(3)	3.2(1)
C23	1.2847(4)	-0.0024(5)	0.2509(2)	3.1(1)
C24	1.3158(4)	-0.0642(6)	0.1921(3)	3.8(1)
C25	1.4396(5)	-0.0648(6)	0.1851(3)	4.7(1)
C26	1.5346(4)	-0.0032(6)	0.2367(3)	4.9(1)
C27	1.5066(5)	0.0598(6)	0.2952(3)	4.7(1)
C28	1.3815(4)	0.0613(5)	0.3013(3)	3.6(1)
N2	1.3289(4)	0.1151(4)	0.3534(2)	4.4(1)
C21	1.2016(5)	0.0904(6)	0.3365(3)	4.0(1)
C32	0.9444(4)	0.0111(5)	0.2843(2)	3.6(1)
C33	0.9275(4)	-0.0646(6)	0.3453(3)	3.9(1)
C34	0.9723(6)	-0.1917(6)	0.3753(3)	5.4(1)
C35	0.9374(6)	-0.2340(8)	0.4367(3)	7.4(2)
C36	0.8596(6)	-0.1540(8)	0.4679(3)	7.9(2)
C37	0.8158(5)	-0.0267(8)	0.4413(3)	6.9(2)
C38	0.8505(5)	0.0175(6)	0.3785(3)	5.0(1)
N3	0.8224(4)	0.1369(5)	0.3386(3)	5.5(1)
C31	0.8788(5)	0.1310(6)	0.2815(3)	4.4(1)

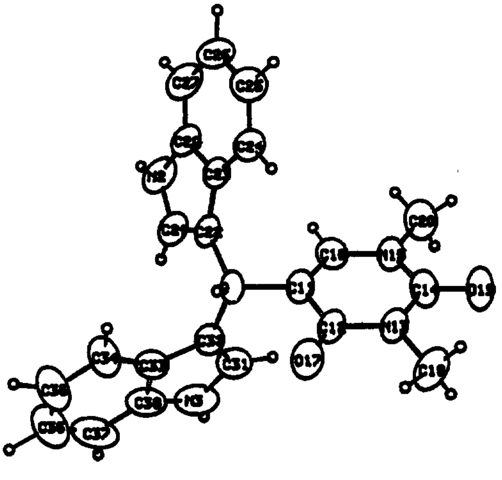

Figure 1. Molecular structure of 3.

Experimental

Melting points are uncorrected. ^{1}H-NMR spectra were measured on a JEOL PMX-60 spectrometer using TMS as an internal standard. IR were measured on a PYE UNICAM, sp3-300 spectrophotometer. Mass spectra were recorded on a 7070E-HE mass spectromter. Column chromatography was carried out on silica gel (Qing Dao 300).

Photoreaction of 5-formyl-1,3-dimethyluracil (1) with indole (2) in the solid state.

The mixed crystal was prepared by melting a mixture of 1 (0.168 g, 0.10 mmol) and 2 (0.351, 0.30 mmol) followed by cooling the melt. The mixed crystal was ground to a

Table 2. Bond distances (Å) and bond angles (°) of **3** with estimated standard deviations in parentheses.

C-N11	1.532(7)	C14-O19	1.239(5)	C27-C28	1.384(7)
C-C22	1.517(6)	C15-C16	1.350(6)	C28-N2	1.366(7)
C-C32	1.518(8)	C15-C20	1.449(8)	N2-C21	1.366(6)
N11-C12	1.459(5)	C22-C23	1.433(7)	C32-C31	1.353(7)
N11-C16	1.351(7)	C22-C21	1.363(6)	C33-C34	1.398(8)
C12-N13	1.395(6)	C23-C24	1.390(7)	C33-C35	1.384(9)
C12-O17	1.221(6)	C23-C28	1.407(6)	C35-C36	1.38(2)
N13-C14	1.383(6)	N3-C31	1.378(8)	C36-C37	1.38(2)
N13-C18	1.482(6)	C25-C26	1.400(7)	C37-C38	1.414(8)
C14-C15	1.344(6)	C26-C27	1.378(8)	C38-N3	1.383(8)

N11-C-C22	111.5(4)	C16-C15-C20	119.8(4)	C-C32-C33	124.6(4)
N11-C-C32	110.4(4)	N11-C16-C15	122.3(4)	C-C32-C31	126.8(5)
C22-C-C32	110.2(4)	C-C22-C23	128.0(4)	C33-C32-C31	108.0(5)
C-N11-C12	117.0(5)	C-C22-C21	125.6(4)	C32-C33-C34	133.9(5)
C-N11-C16	124.1(4)	C23-C22-C21	106.4(4)	C32-C33-C38	106.6(5)
C12-N11-C16	119.0(4)	C22-C23-C24	134.9(4)	C34-C33-C38	119.6(6)
N11-C12-N13	114.6(4)	C22-C23-C28	106.5(5)	C33-C34-C35	118.7(6)
N11-C12-O17	125.2(5)	C24-C23-C28	118.5(4)	C34-C35-C36	121.3(6)
N13-C12-O17	120.4(4)	C23-C24-C25	119.9(4)	C35-C36-C37	122.1(6)
C12-N13-C14	124.6(4)	C24-C25-C26	120.5(5)	C36-C37-C38	117.1(6)
C12-N13-C18	117.2(5)	C25-C26-C27	120.9(5)	C33-C38-C37	121.4(5)
C14-N13-C18	118.1(4)	C26-C27-C28	118.0(4)	C33-C38-N3	107.2(5)
N13-C14-C15	116.8(4)	C23-C28-C27	122.1(5)	C37-C38-N21	131.5(6)
N13-C14-O19	120.1(5)	C23-C28-N2	108.0(5)	C38-N3-C31	109.4(5)
C15-C14-O19	123.0(5)	C27-C28-N2	129.8(4)	C32-C31-N3	108.9(5)
C14-C15-C16	122.5(4)	C28-N2-C21	108.6(4)		
C14-C15-C20	117.7(4)	C22-C21-N2	110.3(5)		

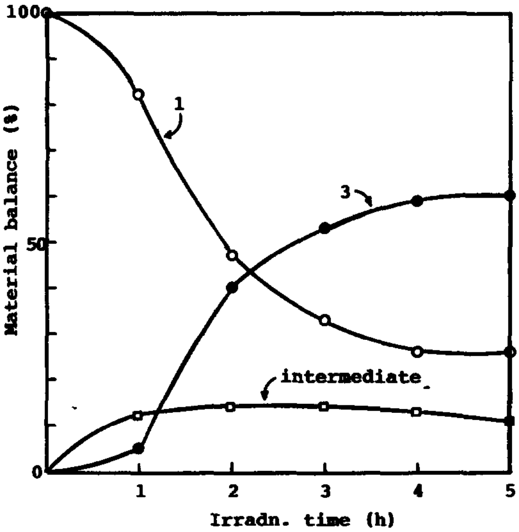

Figure 2. Time course of the photoreaction of **1** in the presence of an excess of **2** in the solid state.

fine powder, spread on the inner wall of a test tube and irradiated with a 300 W high-pressure mercury lamp for 4 h at room temperature. The irradiated mixture was submitted to silica gel column chromatography eluting with chloroform-ethyl acetate (5 : 1) to give **3** (0,154 g; yield 40 %), m.p. 276-277°C; IR (KBr), 3340, 1715, 1610, 760 cm^{-1}; ^{1}H-NMR (DMSO), δ 3.25 (s, 6H, 2 N-Me), 5.90 (s, 1H, C-H), 7.00-7.50 ppm (m, 13H, 11 aromatic and olefinic H, N-H); MS, m/z 384 (M$^+$), 267, 182. Anal. Calcd. for $C_{23}H_{20}N_4O_2$: C, 71.87; H, 5.21; N, 14.58. Found: C, 71.90; H, 5.19; N, 14.50.

Time course of the solid-state photoreaction.

The mixed crystal of **1** and **2** (1 : 4 molar ratio) was irradiated as above and an aliquot was taken time to time and analyzed by HPLC: column, MCH C_{18} reversed phase;

mobile phase, water/methanol (40 : 60); detected at 254 nm. The result is shown in Figure 2.

Photochemical reaction of **1** with **2** in solution.

A solution of **1** (0.168 g, 0.1 mmol) and **2** (0.351 g, 0.3 mmol) in 150 ml of acetonitrile was irradiated with a 300 W high-pressure mercury lamp (Pyrex housing) for 15 h under bubbling nitrogen. After the removal of the solvent in reduced pressure, the residue was submitted to column chromatography (Qing Dao 300 silica gel and elution with 5 : 1 chloroform-ethyl acetate) to give 1,3-dimethyluracil **4** in 20 % yield. When methanol was used as the solvent, **4** was obtained in 65 % yield.

X-ray crystallography.

A colorless crystal of 5-(bis-1-indolyl)methyl-1,3-dimethyluracil (**3**), $C_{23}H_{20}N_4O_2$, having approximate dimensions of 0.3 x 0.3 x 0.3 mm was mounted on a glass fiber in a random orientation. Preliminary examination and data collection were performed with Mo Kα radiation (λ = 0.71073 Å) on an ENRAF-NONIUS CAD4 diffractometer equipped with a graphite crystal incident beam monochromator. A total of 3804 independent reflections were collected in the range of $2 < \theta < 25°$ by ω-2θ scan technique at room temperature, in which 1722 reflections with $I > 3\sigma(I)$ were considered to be observed and used in the succeeding refinement. The corrections for LP factors and for absorption based on a series of Ψ scan were applied to the data.

The crystal is monoclinic, space group $P2_1/n$, with a = 10.831(1), b = 9.650(2), c = 19.355(2) Å, β =102.65(1)°, V = 1973.8 $Å^3$, Mr = 384.44, Z = 4, Dx = 1.29 g/cm^3, μ = 0.80 cm^{-1}, F(000) = 808.

The structure was solved by direct method (MULTAN82). The most of non-hydrogen atoms were located from an E-map. The coordinates of remaining non-hydrogen atoms and hydrogen atoms were found in the succeeding difference Fourier synthesis. The final refinement by full matrix least-square method with anisotropic thermal parameters for non-hydrogen atoms and isotropic thermal parameters for hydrogen atoms was converged with unweighted and weighted agreement factors of 0.052 and 0.051. All calculations were performed on a PDP11/44 computer using SDP-PLUS program system.

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