Sensitized Photooxygenation of Dihydropyrimidines. Formation of a Novel Tetraphenyl-5(4*H*)-pyrimidinone

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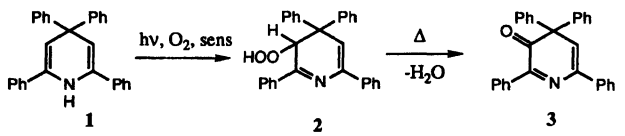
Synopsis. Sensitized photooxygenation of 2,4,4,6-tetraphenyl-1,4(or 3,4)-dihydropyrimidine (**4a**) gave 5-hydroperoxy-2,4,4,6-tetraphenyl-4,5-dihydropyrimidine (**5a**), which was formed by an ene reaction of singlet oxygen with the 1, 4-dihydro form of **4a**. Treatment of **5a** with silica-gel caused dehydration to give 2,4,4,6-tetraphenyl-5(4*H*)-pyrimidinone, which is the first synthesized 5-pyrimidinone.

Previously one of the authors reported that sensitized photooxygenation of 2,4,4,6-tetraphenyl-1,4-dihydropyridine (**1**) afforded 2,4,4,6-tetraphenyl-3(4*H*)-pyridone (**3**) through thermal dehydration of hydroperoxide **2** (Scheme 1).[1] In contrast to 2(1*H*)-pyridones, investigation on synthesis and reactions of 3(4*H*)-pyridone systems such as compound **3** is very limited, and this photochemical transformation of **1** into **3** seems interesting from the synthetic viewpoint. In light of the above, we expected that formation of 5-pyrimidinone may be realized through the photooxygenation of 1,4-dihydropyrimidine which is the 3-aza analog of **1**. While a number of 2-pyrimidinones were widely synthesized and their reactions were investigated,[2] the 5-one system has never been reported. This paper deals with the results of the sensitized photooxygenation of 2,4,4,6-tetraphenyl-1,4(or 3,4)-dihydropyrimidine (**4a**), 4-methyl- (**4b**) and 4-*t*-butyl- (**4c**) derivatives (Chart 1).

Results and Discussion

When an acetone solution of **4a** containing polymer-bound Rose-Bengal (PRB)[3] as a sensitizer was irradiated with visible light under oxygen atmosphere, a photooxygenation product was formed. On monitoring by TLC it was a sole product up to complete conversion of the starting material. The product which was isolated as a pale yellow solid, showed a positive starch–iodine test, indicating that it was a peroxide. Its ^{1}H NMR



Scheme 1.

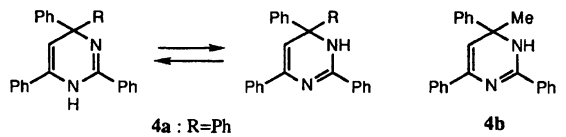


Chart 1.

spectrum exhibited a singlet signal at δ=5.97 which was assigned to 5-H, and an O–H stretching band at 3480 cm^{-1} in the IR spectrum was observed. From these spectral data, this oxygenation product was assumed to be 5-hydroperoxy-2,4,4,6-tetraphenyl-4,5-dihydropyrimidine (**5a**). While peroxide **2** obtained from **1** was easily dehydrated in solution at room temperature,[1] on crystallization from acetone **5a** gave a plate-like single crystal, in which acetone was included with a ratio of 1 : 1. From the X-ray structure analysis of the crystal the structure of **5a** was confirmed (Fig. 1). Probably **5a** was produced by an ene reaction of singlet oxygen and **4a** in 1,4-dihydro form as in the formation of **2** from **1**.

When **5a** was treated with silica-gel, it was transformed into a violet crystalline product. The IR spectrum of it showed a strong carbonyl stretching band at 1710 cm^{-1}, and in the mass spectrum the molecular ion peak was observed at *m/z* 400, indicating that the product was formed by dehydration of **5a**. Based on these spectral data and an analogy with the formation of pyridinone **3** from **2**, the dehydrated product was assigned to be 2,4,4,6-tetraphenyl-5(4*H*)-pyrimidinone (**6**) (Scheme 2). The electronic spectrum of **6** in hex-

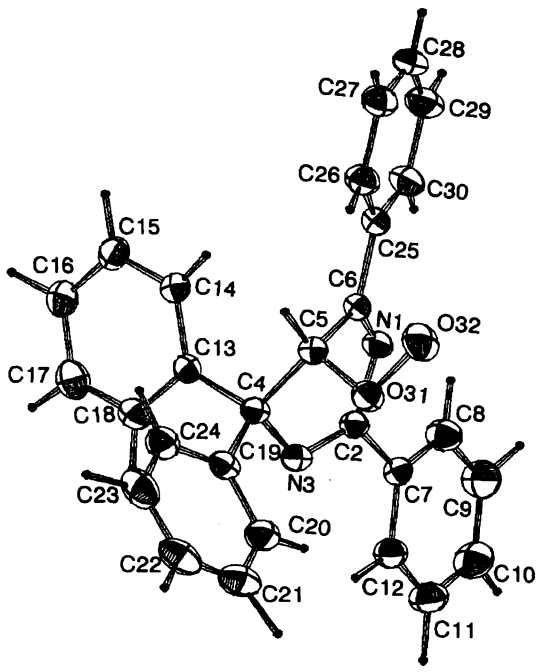


Fig. 1. ORTEP[12] plot of **5a** with the atom-numbering. The anisotropic ellipsoids for non-H atoms enclose 30% probability.

ane showed an n, π^* absorption band around 540 nm, which is largely red-shifted in comparison with that of **3** (λ_{max}=460 nm).

Next, 4-methyl derivative **4b** was irradiated in acetone in the presence of PRB. An oxygenation product was obtained as a pale yellow powdery solid. Its ^{1}H NMR spectrum showed a singlet at δ=5.34 and a methyl-proton signal at δ=1.96. Considering the spectral similarity with **5a**, this product can be assigned to be the corresponding hydroperoxide, 5-hydroperoxy-4-methyl-2,4,6-triphenyl-4,5-dihydropyrimidine (**5b**), but the relative stereochemistry at the 4- and 5-positions is undetermined. In order to get further evidence for its structure **5b** was treated with triethyl phosphite in toluene. Although the product was not completely separated from remaining triethyl phosphite, the ^{1}H NMR spectrum suggested that **5b** should be reduced to alcohol **7**. Dehydration of **5b** with silica-gel was attempted, but **5b** decomposed into a mixture of unidentified products and the corresponding 5-pyrimidinone was not obtained. Treatment of **5b** with K_2CO_3 or *p*-toluenesulfonic acid also gave complex mixture.

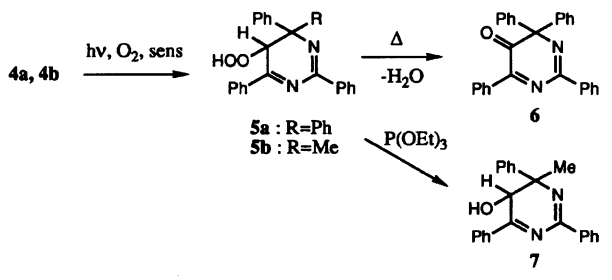
Reaction of 4-*t*-butyl derivative **4c** and singlet oxygen was also carried out in acetone. In this case, the corresponding hydroperoxide was not formed, but another product was isolated and identified as 2,4,6-triphenylpyrimidine (**8**) based on mp and spectral data.[4]

Thus, a novel heterocyclic ketone, 5(4*H*)-pyrimidinone **6** was synthesized for the first time from dihydropyrimidine **4a** via dye-sensitized photooxygenation and successive dehydration. This photochemical transformation, however, was influenced by the kind of substituents at the 4-position.

Experimental

IR and UV spectra were recorded with a JASCO A-3 spectrometer and a Shimadzu UV240 spectrophotometer, respectively. ^{1}H NMR spectra (270 MHz) were obtained on a JEOL JNM-GX270 spectrometer in $CDCl_3$ with tetramethylsilane as internal standard. Mass spectrum (EI, 70 eV) was recorded on a JEOL DX-300 mass spectrometer. Mps were obtained with a Yanagimoto micro apparatus and are uncorrected.

Materials. **4a—c** were synthesized from 2,4,6-triphenylpyrimidine[4] and an appropriate organolithium reagent by the method of Cook et al.[5] Mp and spectral data of **4a**[6] and **4b**[5] coincided with the reported values.



Scheme 2.

4-*t*-Butyl-2,4,6-triphenyl-1,4(or 3,4)-dihydropyrimidine (**4c**). Yield 19%. Mp 184.5—186 °C; UV (EtOH) 320 (ε 2300) and 232 (29000) nm; IR (KBr) 3450 (ν_{NH}), 1680, 1640 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.17 (9H, $CH_3\times3$), 5.63 (0.5H, s, 5-H), 6.14 (0.5H, br s, NH), 6.18 (0.5H, s, 5-H), 6.65 (0.5H, br s, NH), 7.2—8.1 (15H, m, ArH); MS *m/z* (rel intensity) 351 (M^+-CH_3; 0.8), 309 (100), 104 (30).

Photooxygenation of 4a. Pyrimidine **4a** (107 mg) in acetone (70 mL) containing PRB (100 mg) was irradiated at 5—10 °C with a 400 W xenon lamp through a Toshiba glass filter Y-47 (λ>450 nm). During the irradiation oxygen was bubbled through the solution. After the starting material was almost consumed (ca. 8h), PRB was filtered off, the solvent was removed under reduced pressure, and the residue was recrystallized from hexane–ether to give **5a**: Mp 119—120 °C (decomp); IR (KBr) 3480 cm^{-1} (ν_{OH}); ^{1}H NMR δ=5.97 (s, 1H, 5-H), 7.1—7.6 (m, 14H), 7.73 (br s, 1H, exchangeable in D_2O), 7.83 (d, 2H, J=8.5 Hz), 8.3 (m, 2H), 8.5 (m, 2H).

On the other hand, when the filtrate was concentrated and cooled, acetone solvate of **5a** was deposited as yellow plate-like crystals [Mp 95—98 °C (decomp)].

Isolation of 2,4,4,6-Tetraphenyl-5(4*H*)-pyrimidinone (6). **5a** was chromatographed on a silica-gel (Wacogel C-200) column using benzene as eluent. Reddish violet fractions were collected and evaporated to give **6** (35% from **4a**) as violet needles; mp 183.5—184.5 °C (from hexane); UV (hexane) 540 nm (ε 150); IR (KBr) 1710 cm^{-1} (C=O); ^{1}H NMR δ=7.2—7.5 (m, 16H), 8.2 (m, 2H), 8.5 (m, 2H); MS *m/z* (rel intensity) 400 (M^+; 19%), 269 (100), 166 (64), 165 (89). HRMS: *m/z* 400.1552. Calcd for $C_{28}H_{20}N_2O$: M, 400.1576.

X-Ray Structure Determination of 5a. Crystal data: $C_{28}H_{22}N_2O_2\cdot C_3H_6O$, M_r=476.56, monoclinic, $A2/a$, a=25.318 (5), b=18.556 (4), c=11.008 (5) Å, β=95.61 (2)°, V=5147 (3) Å^3, Z=8, D_x=1.230 g cm^{-3}, λ(Mo $K\alpha$)=0.71073 Å, μ=0.74 cm^{-1}, F(000)=2016. Intensity data were collected on a Rigaku AFC-5 four-circle diffractometer with graphite-monochromated Mo $K\alpha$ radiation using the ω–2θ scan technique up to 2θ=50.0°. 4754 Reflections were measured and 3478 with $|F_o|>3\sigma(|F_o|)$ were considered as observed and used for structure determination. The structure was solved by direct methods (MULTAN78[7]) and refined by full-matrix least-squares (SHELX76[8]). The atoms of acetone were disordered between two sets of positions and refined isotropically with each occupancy factor fixed to be 0.5.[9] The final refinement with anisotropic thermal parameters for non-H atoms of **5a** and isotropic ones for atoms of acetone molecules and H-atoms of **5a** converged at R=0.059 and R_w=0.070 for 3478 observed reflections. Atomic scattering factors were taken from International Tables for X-Ray Crystallography.[10] Calculations were carried out on an IBM 4381-R24 computer at Ochanomizu University.[11]

Photooxygenation of 4b. An acetone solution (40 ml) of **4b** (39 mg) containing PRB (56 mg) was irradiated under the same condition as in the case of photooxygenation of **4a**. After irradiation for 8 h, PRB was filtered off, and the filtrate was concentrated and then diluted with hexane to give crude **5b** (34 mg, 79%) as cream-yellow powdery solid. ^{1}H NMR δ=1.96 (s, 3H, Me), 5.34 (s, 1H, 5-H), 7.1—7.6 (m), 8.08 (m, 2H), 8.43 (m, 2H).

Reduction of 5b into 7. Photooxygenation of **5b**

(16.5 mg) was carried out as described above and the solvent was removed with a rotary evaporator. The residue was dissolved into 10 mL of toluene and 50 mg of triethyl phosphite was added. The reaction mixture was stirred at room temperature for 3 h, concentrated under reduced pressure, and diluted with hexane to give crude **7** as yellow solid (8.6 mg). Since **7** was decomposed on silica-gel further purification was not succeeded. ^{1}H NMR ($CDCl_3$) δ=1.86 (3H, s, CH_3), 2.0 (1H, br d, exchangeable in D_2O), 4.86 (1H, br d, 5-H), 7.1—7.6 (m), 8.04 (2H, m), 8.44 (2H, m).

Photooxygenation of 4c. Photolysis of **4c** (15 mg) was carried out by similar procedures. After irradiation for 7 h, PRB was filtered off and the filtrate was concentrated to give the product as colorless needles (4 mg), which was identified as 2,4,6-triphenylpyrimidine since the mp and IR spectrum coincided with that of authentic sample.

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