

Photo-oxygenation of 2,4,4,6-Tetraphenyl-1,4-dihydropyridine

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Sensitized photo-oxygenation of 2,4,4,6-tetraphenyl-1,4-dihydropyridine (1) in acetone or cyclic ethers gave an unstable peroxide which was assumed to be 3-hydroperoxy-2,4,4,6-tetraphenyl-3,4-dihydropyridine (2). The peroxide (2) easily decomposed to give 2,4,4,6-tetraphenyl-3-pyridone (3). In aromatic hydrocarbons or methylene dichloride, sensitized photo-oxygenation of (1) afforded two products, (4) and (5). The product (4) was a stable hydroperoxide which was determined to be *N*-(2-hydroperoxy-4-oxo-1,3,3-triphenylbutan-1-ylidene)benzamide. The product (5) was not a peroxide, and it was assigned the structure 3-hydroxy-2,4,4,6-tetraphenyl-3,4-dihydropyridine. Possible mechanisms are suggested for the formation of the reaction products.

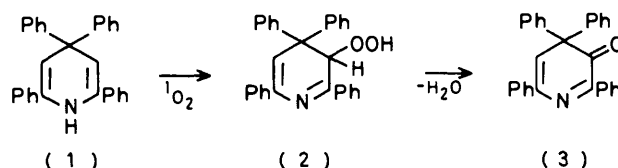
During the course of an investigation of the photochemical colouration of 2,4,4,6-tetraphenyl-1,4-dihydropyridine (1) under irradiation with u.v. light in deaerated solutions,¹ we found that (1) is sensitive to oxygen present in the solutions particularly in benzene, and colouration does not occur. In order to clarify the reaction products of (1) with oxygen, sensitized photo-oxygenation and autoxidation in several solvents were studied. Three new oxygenation products, (3), (4), and (5), were isolated and identified. We report here the results of structural studies on these compounds.

Results and Discussion

Sensitized photo-oxygenation of compound (1) in acetone containing Rose Bengal or polymer-bound Rose Bengal² as a sensitizer at 5 °C gave a colourless unstable peroxide (2); monitoring of the reaction by t.l.c. showed this to be the sole product. The peroxide (2) decomposed gradually on standing in the dark at -20 °C, and very quickly at slightly higher temperatures or on treatment with ethanol, to give orange prisms of the ketone (3). Elemental analysis and mass spectrum [*m/e* 399 (*M*⁺)] of (3) gave the molecular formula C₂₉H₂₁NO. The i.r. spectrum showed a characteristic carbonyl band at 1 702 cm⁻¹, and the ¹H n.m.r. spectrum a characteristic olefinic proton resonance at 6.71 p.p.m.; the structure of (3) was thus determined to be 2,4,4,6-tetraphenyl-3-pyridone. Therefore its precursor, the peroxide (2), was assumed to be 3-hydroperoxy-2,4,4,6-tetraphenyl-3,4-dihydropyridine, produced by an ene reaction of (1) with singlet oxygen; on warming, this hydroperoxide breaks down to the dehydration product (3), as shown in Scheme 1. Sensitized photo-oxygenation of (1) in cyclic ethers, such as dioxan or tetrahydrofuran (THF), also gave the hydroperoxide (2).

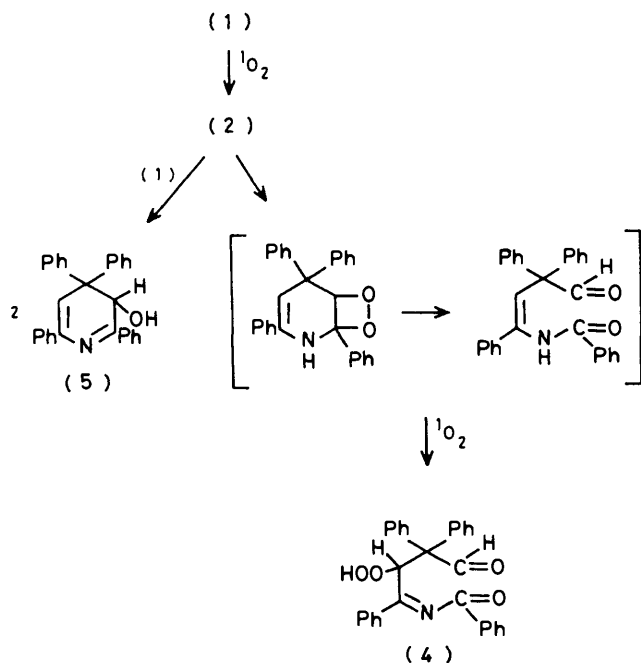
Control experiments, *i.e.* either in the dark, or without a sensitizer, showed no detectable change in compound (1) after *ca.* 5 h. However, after 2 weeks, with occasional flushing with oxygen in the dark, the reaction mixture showed a positive starch-iodine test, and a small amount of a peroxide different from (2) was isolated. This product was found to be identical with the compound (4) obtained by the photo-oxygenation of (1) in aromatic hydrocarbons, which will be described below.

Sensitized photo-oxygenation of the pyridine (1) in benzene was carried out at 7 °C or 20 °C in the presence of Rose Bengal supported on silica gel³ as sensitizer. Monitoring of the reaction by t.l.c. showed that in both cases three products, different from either (2) or (3), were formed, although the reaction rate at 20 °C was faster than that at 7 °C. Two of the products, a major one, (4), and a minor one, (5), were isolated as colourless prisms and colourless needles, respectively. The



Scheme 1

product (4) showed a positive starch-iodine test indicating it to be a peroxide, whilst (5) gave a negative result. The peroxide (4), recrystallized from benzene, was surprisingly stable and could be stored at room temperature, in the dark, without appreciable decomposition for several weeks. The elemental analysis, mass spectrum [*m/e* (C.I.) 525 (*M*⁺)], and the number of phenyl protons which appeared in the n.m.r. spectrum of (4) (recrystallized from benzene) strongly suggested that one molecule of benzene had been incorporated in each product molecule. In a measurement of the thermal gravity differential thermal analysis (TGDTA) of (4), recrystallized from benzene, about 15% of the weight was lost between 50 and 100 °C. The loss was presumed to be due to the liberation of one mole of incorporated benzene. The resulting sample lost about another 6% of the weight between 120 and 160 °C, and then decomposed with exotherms, indicating the liberation of two oxygen atoms followed by combustion with the oxygen. The observations confirmed the fact that the peroxide (4) crystallizes with one molecule of solvent benzene; solvent-free (4) was obtained by heating the solvent-containing crystals at 100 °C under reduced pressure until constant weight was reached. Elemental analysis of solvent-free (4) gave the molecular formula C₂₉H₂₃NO₄, while iodometric titration⁴ supported the presence of one peroxy group. Its n.m.r. spectrum exhibited three singlets at 9.51, 8.65, and 6.65 p.p.m., assigned to the formyl, hydroperoxy, and CH protons, respectively. The i.r. spectrum of benzene-containing (4) showed the characteristic carbonyl band of a formyl group at 1 720 cm⁻¹; however, solvent-free (4) showed a doublet structure for the carbonyl absorption of the formyl group, at 1 700 and 1 720 cm⁻¹, in which the intensity of the absorption at 1 700 cm⁻¹ was stronger than that at 1 720 cm⁻¹. The stronger band was assumed to result from a transannular amide-type neutralization between the formyl carbon and the benzoylimino-nitrogen,⁵ which was probably enhanced by the liberation of the solvent benzene. From these observations, (4) was assigned the structure *N*-(2-hydroperoxy-4-oxo-1,3,3-triphenylbutan-1-ylidene)benzamide. Although the singlet absorption at 6.65 p.p.m., which was assigned to a CH proton at the 2-position, was shifted further downfield than the



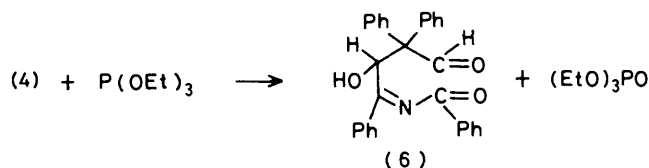
Scheme 2

expected value, 4.9 p.p.m.,⁶ a molecular model of (4) showed that this hydrogen can be affected by strong anisotropic deshielding effects⁷ from the two phenyl groups in the 1- and 3-positions.

A possible mechanism for the formation of the peroxide (4) is shown in Scheme 2. The fact that (4) is produced by controlled, sensitized photo-oxygenation of (2) in benzene seems to support a mechanism for the direct formation of (4) by photo-oxygenation of (1) which involves compound (2).

In order to confirm the structure of (4), deoxygenation of the hydroperoxy-group was carried out. When it was treated with triethyl phosphite in toluene, colourless prisms of the benzamide (6) were obtained. The elemental analysis and mass spectrum [m/e 434 ($M^+ + 1$)] of (6) gave the molecular formula $C_{29}H_{23}NO_3$, while its i.r. spectrum also showed a doublet carbonyl absorption, at 1 708 and 1 720 cm^{-1} , which was assigned to a formyl group closely resembling that of compound (4). The n.m.r. spectrum of (6) exhibited three singlets, at 9.35, 6.65, and 2.18 p.p.m., which were assigned to the formyl, CH, and hydroxy-protons, respectively. Although two doublets in the n.m.r. spectrum, expected from coupling between the hydroxy-proton and the 2-hydrogen on the same carbon, were not present, the structure of (6) was assumed to be *N*-(2-hydroxy-4-oxo-1,3,3-triphenylbutan-1-ylidene)benzamide (Scheme 3).

The product (5), which did not show a starch-iodine test, was not a peroxide. Its n.m.r. spectrum showed two doublets at 4.9 and 0.9 p.p.m. in $CDCl_3$, attributed to the 3-hydrogen and the hydroxy-proton on the same carbon, coupling with each other, and two singlets at 6.12 p.p.m. (olefinic proton) and 1.5 p.p.m. Because crystals of (5), recrystallized from benzene, were found to contain about 1 mole of solvent benzene, elemental analysis and molecular weight determination (m/e 419) were carried out after the crystals had been dried at 100 °C under reduced pressure until constant weight was reached. From these results the molecular formula of (5) was determined to be $C_{29}H_{25}NO_2$. The formula suggested incorporation of one molecule of water, and the singlet absorption (exchangeable in D_2O) which appeared at 1.5



Scheme 3

p.p.m. in the n.m.r. spectrum was assigned to this. In the TGDTA measurement, no loss of weight was observed before endothermic melting at 129 °C, indicating that the water molecule was retained with unusual tenacity.* From these observations (5) was assumed to be 3-hydroxy-2,4,4,6-tetraphenyl-3,4-dihydropyridine monohydrate.

Autoxidation of (1) in oxygen-saturated benzene in the dark at 20 °C for 3 days also gave compounds (4) and (5), identical with the products in the sensitized photo-oxygenation, which suggested participation of triplet oxygen in the photo-oxygenation. However, the formation of (4) was greatly inhibited by addition of 1,4-diazabicyclo[2.2.2]octane as a singlet-oxygen quencher in the sensitized photo-oxygenation of (1). Therefore, under the conditions of sensitized photo-oxygenation, singlet oxygen appears to react with the pyridine (1) to give the benzamide (4) *via* the hydroperoxide (2). When a concentrated benzene solution of compound (1) was left in the dark for about 1 month without flushing with oxygen, compound (5) was isolated in good yield (20%) together with unchanged (1). This observation suggests that in a solution in which the oxygen concentration is low and the concentration of (1) is high, compound (5) is formed by an interaction between (1) and (2), whereas in a solution in which the oxygen concentration is high, (2) reacts further with oxygen to give (4), as shown in Scheme 2.

Sensitized photo-oxygenation of (1) in either toluene or methylene dichloride gave solvent-free (4) as a major product together with a minor amount of (5). Another minor product which appeared on t.l.c., mentioned above, which we have been unable to isolate in a pure state, was not a peroxide.

Experimental

I.r. spectra were recorded with a JASCO A-3 spectrometer. 1H n.m.r. spectra were obtained with a JEM C-60HL spectrometer with tetramethylsilane as internal standard unless otherwise indicated. Mass spectra were run on a Hitachi RMU-6MC or RMU-7M spectrometer. TGDTA measurements were carried out with an ULVAC TGD-300 instrument with Al_2O_3 as standard. M.p.s were obtained with a Yanagimoto micro melting-point apparatus unless otherwise indicated, and are all uncorrected.

Starting Materials.—The dihydropyridine (1) was synthesized by the method of Calvalho⁸ and recrystallized from benzene under nitrogen in the dark to give colourless needles, m.p. 234–235 °C; ν_{max} (KBr) 3 400 and 1 670 cm^{-1} ; λ_{max} (EtOH) ($\epsilon \times 10^4$) 210 (4.5), 238 (2.9), 290 (5.8×10^{-1}), and 330 nm (7.7×10^{-2}); $\delta(C_6D_6)$ 5.15 (br s, 1 H, exchangeable in D_2O), 5.30 (s, 2 H), and 7.0–8.2 (m, 20 H). Polymer-bound Rose Bengal (P-RB) was prepared according to the method of Schaap *et al.*² from Rose Bengal (1.58 g) and chloromethylated polystyrene (containing 2% of divinyl benzene,

* Similar cases in which solvent molecules are retained with unusual tenacity in crystals were reported for triaryldihydrotriazines, the molecular structures of which resemble that of (5) (H. Anker and H. Cook, *J. Chem. Soc.*, 1941, 323).

100–200 mesh, 2.0 g). Rose Bengal supported on silica gel (S-RB) was prepared by the method of Nilson and Kearns³ from Rose Bengal (200 mg) and Wakogel C-200 (100–200 mesh, 8 g).

General Procedure for Sensitized Photo-oxygenation.—All irradiations were performed in solvents (100 ml) with a sensitizer. This sensitizer was most frequently Rose Bengal, but P-RB was also used in order to facilitate removal of the sensitizer from the reaction mixture in acetone, THF, or dioxan. In aromatic hydrocarbons or methylene dichloride, S-RB was more frequently used as sensitizer than P-RB. Oxygen was bubbled slowly through solutions under irradiation with a 300-W tungsten lamp in a thermostatically controlled bath with a Coolnics circulator CTE 220. After irradiation, S-RB or P-RB was filtered off, and Rose Bengal was removed by recrystallization of the products. Photo-oxygenations were monitored by silica-gel t.l.c. (benzene–acetone, 40 : 1). The yield of products was based on isolated materials.

Isolation of 2,4,4,6-Tetraphenyl-3-pyridone (3).—A solution of compound (1) (0.1 g) in acetone containing Rose Bengal was irradiated while oxygen was bubbled through at 5 °C. Monitoring by t.l.c. showed that (1) was consumed within *ca.* 1 h. The residual solid (2), obtained after the removal of the solvent under reduced pressure at around 0 °C, showed a positive starch–iodine test. It was then washed with ethanol to remove Rose Bengal which was incorporated at around 5 °C and gave an orange solid (3). When P-RB was used as a sensitizer, the colourless solid (2) (decomp. 82–86 °C) was obtained. On treatment with ethanol or on heating, this solid (2) gave the orange solid (3). Recrystallization from ethanol–acetone gave orange prisms of (3) (49%), m.p. 171–172 °C; ν_{\max} (KBr) 1702 cm^{-1} ; λ_{\max} (EtOH) (ϵ) 390 (5.4×10^2), 310 (5.7×10^3), and 220 nm (1.8×10^4); $\delta(\text{CDCl}_3)$ 6.71 (s, 1 H) and 7.3–8.0 (m, 20 H) (Found: C, 86.65; H, 5.3; N, 3.45. Calc. for $\text{C}_{29}\text{H}_{21}\text{NO}$: C, 87.22; H, 5.26; N, 3.51%); *m/e* 399 (M^+).

Isolation of N-(2-Hydroperoxy-4-oxo-1,3,3-triphenylbutan-1-ylidene)benzamide (4) and 3-Hydroxy-2,4,4,6-tetraphenyl-3,4-dihydropyridine Monohydrate (5).—A solution of compound (1) (0.5 g) in benzene containing S-RB (0.5 g) was irradiated and oxygen bubbled through at 20 °C for *ca.* 2 h. After irradiation, S-RB was filtered off and the filtrate was concentrated under reduced pressure. When the resulting solution was left for one night (or longer), crystals of (4) were precipitated which showed a positive starch–iodine test. These were filtered off, and compound (5) was then precipitated from the filtrate by addition of a small amount of ethanol. Colourless prisms of (4) obtained by recrystallization

from benzene were dried at 100 °C under reduced pressure until constant weight was reached. Colourless needles of (5), also obtained by recrystallization from benzene, which did not show a positive starch–iodine test, were dried at 100 °C under reduced pressure until constant weight was reached. Compound (4) (35%), m.p. 157–160 °C (decomp.; from TGDTA measurement), ν_{\max} (KBr) 3380, 2950, 2850, 1720, 1700, and 1633 cm^{-1} ; $\delta(\text{CDCl}_3)$ * 9.51 (s, 1 H), 8.65 (s, 1 H, exchangeable in D_2O), 8.05–7.20 (m, 20 H), and 6.65 (s, 1 H) (Found: 77.6; H, 5.1; N, 3.15. Calc. for $\text{C}_{29}\text{H}_{23}\text{NO}_4$: C, 77.50; H, 5.12; N, 3.17%). Compound (5) (4%), m.p. 136–137 °C (from TGDTA measurement), ν_{\max} (KBr) 3370 cm^{-1} ; $\delta(\text{CDCl}_3)$ 7.8–6.8 (m, 20 H), 6.12 (s, 1 H), 4.9 (d, *J* 9 Hz, 1 H, changed to a singlet in D_2O), 1.50 (s, 2 H, exchangeable in D_2O), 0.9 (d, *J* 9 Hz, exchangeable in D_2O) (Found: C, 83.1; H, 5.7; N, 3.35%. Calc. for $\text{C}_{29}\text{H}_{23}\text{NO}\cdot\text{H}_2\text{O}$: C, 83.05; H, 5.97; N, 3.34%); *m/e* 419 (M^+).

Preparation of N-(2-Hydroxy-4-oxo-1,3,3-triphenylbutan-1-ylidene)benzamide (6) from the Hydroperoxide (4).—Triethyl phosphite (66 mg) was added to a solution of (4) (100 mg) in toluene (40 ml), and the mixture left overnight at room temperature. The solvent and the excess of triethyl phosphite were then removed under reduced pressure to give a crystalline solid (6), showing no starch–iodine test. Recrystallization from benzene afforded colourless prisms (66%), m.p. 219–220 °C; ν_{\max} (KBr) 3530, 3380, 2950, 2850, 1720, 1708, and 1635 cm^{-1} ; $\delta(\text{CDCl}_3)$ 9.35 (s, 1 H), 7.95–6.85 (m, 20 H), 6.65 (s, 1 H), 2.18 (s, 1 H, exchangeable in D_2O) (Found: C, 80.05; H, 5.35; N, 3.2. Calc. for $\text{C}_{29}\text{H}_{23}\text{NO}_3$: C, 80.37; H, 5.31; N, 3.23%); *m/e* 434 ($M^+ + 1$).

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* This measurement was carried out with JNM FX-200 spectrometer.