Regioselective Photo-oxygenation of 2-Aryl-4,5,6,7-tetrahydroindoles: Preparation and Reactions of 2-Aryl-7a-hydroperoxy-4,5,6,7,7a-pentahydroindolenines

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Dye-sensitized photo-oxygenation of 2-aryl-4,5,6,7-tetrahydroindoles quantitatively afforded 2-aryl-7a-hydroperoxy-4,5,6,7,7a-pentahydroindolenines, which were converted into the corresponding hydroxy-indolenines and spiro-γ-lactams in excellent yields.

Dye-sensitized photo-oxygenation of pyrroles has been widely investigated during the last 2 decades.[1-7] However, in this photoreaction, a variety of oxidation products or complex mixtures were generally produced in a non-selective manner except in the cases of poly-phenyl- and poly-t-butyl-substituted pyrroles.[6,7] We now report the regioselective photo-oxygenation of bicyclic pyrroles such as 2-aryl-4,5,6,7-tetrahydroindoles (**1a**—**d**) to give stable hydroperoxy compounds (**2a**—**d**) at room temperature.

Irradiation of methanolic solutions of (**1a**—**d**) containing methylene blue as sensitizer under a continuous stream of oxygen gas with a 300 W halogen lamp for 20—30 min regioselectively gave 2-aryl-7a-hydroperoxy-4,5,6,7,7a-pentahydroindolenines (**2a**—**d**) in quantitative yield (Scheme 1).† No solvent-incorporated product was detected *via* its endoperoxide even at low temperature ($\leqslant -50$ °C).

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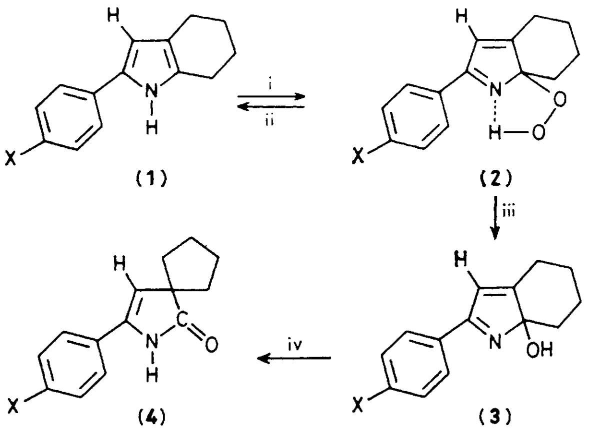
† After evaporation of methanol below 30 °C, the residue was dissolved in benzene–hexane(1 : 1). Insoluble methylene blue was filtered off and evaporation of the solvent below 30 °C gave the hydroperoxide as a colourless solid in a practically pure state.



a; X = H
b; X = Me
c; X = Cl
d; X = Br

Scheme 1. i, *h*ν-methylene blue, O_2, MeOH; ii, $NaBH_4$, MeOH; iii, PPh_3 or Me_2S; iv, heat or $KOBu^t$–DMF.

For the formation of (**2a**), tetraphenylporphyrin was also effective as a sensitizer. However, a complex mixture was obtained when rose bengal or Ru(bpy)$_3^{2+}$ (bpy = bipyridine) was used. It was also found that MeCN, CH_2Cl_2, and C_6H_6 can be used as solvents. The oxidation of (**1a**) by $NaOCl$–H_2O_2 in an aqueous methanolic solution afforded the hydroperoxide (**2a**) in the dark. The formation of (**2a**) in the methylene blue-sensitized photoreaction was quenched by 1,4-diazabicyclo-[2.2.2]octane or β-carotene efficiently. These results clearly suggest that $^1O_2$ is an active species for the photo-oxidation.

The structures of (**2a**—**d**) were assigned from their elemental analyses and spectral properties,‡ and also from chemical transformations including the positive peroxide test.

The hydroperoxides (**2a**—**d**) were stable at room temperature ($\leqslant$35 °C) for at least 10 days. The reduction of (**2a**—**d**) with PPh_3 in Et_2O or Me_2S in MeOH gave 2-aryl-7a-hydroxy-4,5,6,7,7a-pentahydroindolenines (**3a**—**d**) in quantitative yields.‡ In contrast, the reduction of (**2a**) with $NaBH_4$ in MeOH afforded the starting pyrrole (**1a**) in a quantitative yield. The other unusual observation was that the spiro-γ-lactams (**4a**—**d**) are obtained in excellent yields (80—90%) *via* 1,5-sigmatropic rearrangement on pyrolysis of (**3a**—**d**) at 180 °C for 3 min under an argon atmosphere or on treatment with $KOBu^t$ in *N*,*N*-dimethylformamide at −30 °C for 1 h.‡

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‡ Compound (**2a**): m.p. 126—128 °C (decomp.); u.v. λ_{max}(MeOH) 252 nm (ε 14 000); i.r. ν_{max}(KBr) 3040, 2840—2740 (OOH ··· N), 1640 (C=N), and 1600 cm^{-1}; *m*/*z* 213 ($M^+ - 16$); ^{1}H n.m.r. δ($CDCl_3$) 8.80—3.05(8H, m, CH_2), 6.40(1H, s, CH=C), 7.00—7.60 (5H, m, Ph), and 12.00(1H, br., OOH). Compound (**3a**): m.p. 154—155 °C (decomp.); u.v. λ_{max}(MeOH) 252 nm(ε 17 200); i.r. ν_{max} (KBr) 3080(OH), 1635 (C=N) cm^{-1}; *m*/*z* 213(M^+); the ^{1}H n.m.r. spectrum of (**3a**) was not obtained owing to its insolubility in $CDCl_3$ and $(CD_3)_2SO$. Compound (**4a**): m.p. 181—182 °C; i.r. ν_{max}(KBr) 3140(NH), 1680(C=O) cm^{-1}; *m*/*z* 213(M^+); ^{1}H n.m.r. δ($CDCl_3$) 1.40—2.10(8H, m, CH_2), 5.65(1H, d, *J* 2 Hz, CH=C), 7.20—7.60(5H, m, Ph), 9.45(1H, br., NH); ^{13}C n.m.r. δ($CDCl_3$) 26.1(t), 36.5(t), 57.4(s), 111.6(d), 124.7(d), 128.6(d), 128.8(d), 130.3(s), 138.0(s), and 187.0(s) p.p.m. All new compounds gave satisfactory elemental analyses.