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PHOTOREDUCTION OF QUINOLINE METHANOLS

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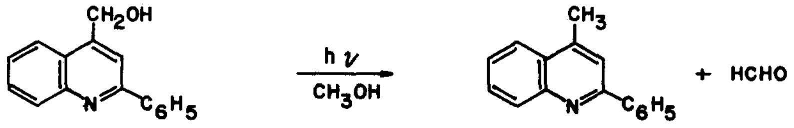
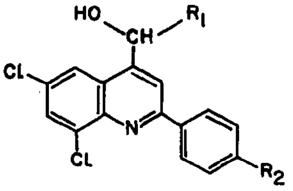
2-Phenyl-4-quinoline methanols bearing a variety of side chains and nuclear substituents have shown promise as antimalarial drugs[1] but their usefulness has been vitiated by pronounced phototoxicity[1]. In this connection, we have investigated[2] the action of light upon such compounds and have observed photoreduction of the free bases in methanol solution.

Irradiation of degassed[3] solutions of 2-phenyl-4-quinoline methanol[4] (I) at 3130 Å resulted in disappearance of starting material with a quantum yield of 10^{-3} - 10^{-4}. Preparative irradiations[5] using Pyrex equipment and 1.2×10^{-2} M degassed solutions of I produced a non-volatile product (> 95% yield) shown to be 2-phenyl-4-methyl quinoline (II) by comparison with an authentic[6] sample. In addition to II, formaldehyde was produced in 85% yield. Formation of II was also observed when degassed solutions of I were irradiated at 2537 Å. Other, unidentified, products were also formed and II was slowly consumed upon prolonged irradiation at this wavelength.

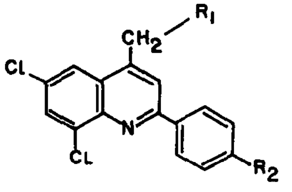


I II

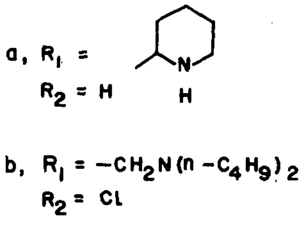
Irradiations of the phototoxic anti-malarials α-[2-piperidyl]-2-phenyl-6,8-dichloro-4-



III a, b

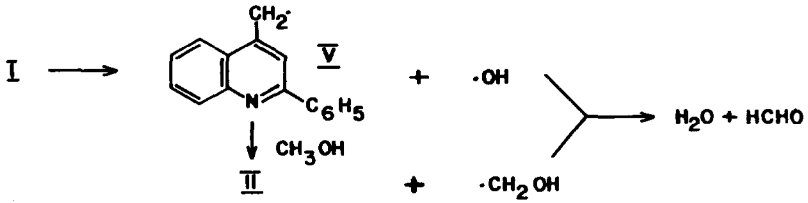


IV a,b



quinoline methanol (IIIa) and α-[di-n-butylaminomethyl]-2-phenyl-4',6,8-trichloro-4-quinoline methanol (IIIb) under similar conditions also produced formaldehyde (80% yield) and deoxycompounds[7] (IVa, b). Irradiation of 4-hydroxymethylpyridine or benzyl alcohol at 2537 Å did not produce γ-picoline or toluene.

After most of this work had been completed, Stenberg et al[8] reported an analogous reaction of quinine and related compounds in acidic solution. A mechanism involving hydrogen abstraction by diprotonated quinine and eventual elimination of water was suggested. Such a mechanism appears unlikely in the present work where methanol solutions of the free bases were irradiated. A more reasonable alternative might be homolytic cleavage of photoexcited[9] I (or III) to hydroxyl and "benzyl" (V) radicals followed by H-abstraction from methanol to form II (or IV) and a hydroxymethyl radical. Formaldehyde and water would then be produced from hydroxyl and hydroxymethyl radicals.



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2. Cf. M.B. Rubin, U.S.Govt.Res.Develop.Rep., 69, 55 (1969); Chem. Abstr., 71, 73976y (1969).
3. Degassing was performed by five freeze-pump-thaw cycles on a high vacuum line.
4. K.W. Rosenmund and F. Zymalkowski, Chem. Ber., 85, 152 (1952).
5. Degassed solutions in methanol in a Pyrex vessel were irradiated with unfiltered light from a 1000 w, high-pressure mercury vapor lamp (GE AH-6). Irradiation times averaged one hour per mg for complete disappearance of starting material.
6. D.S. Tarbell, J.F. Bunnett, R.B. Carlin, and V.P. Wystrach, J.Amer.Chem.Soc., 67, 1582 (1945).
7. These reactions were complicated by partial loss of the nuclear chlorine substituents.
8. V.I. Stenberg, E.F. Travecedo, and W.E. Musa, Tetrahedron Letters, 2031 (1969).
9. Marked inhibition by oxygen is suggestive of a triplet state reaction.