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A NEW PHOTOREDUCTION ON QUINOLINE ALKALOIDS

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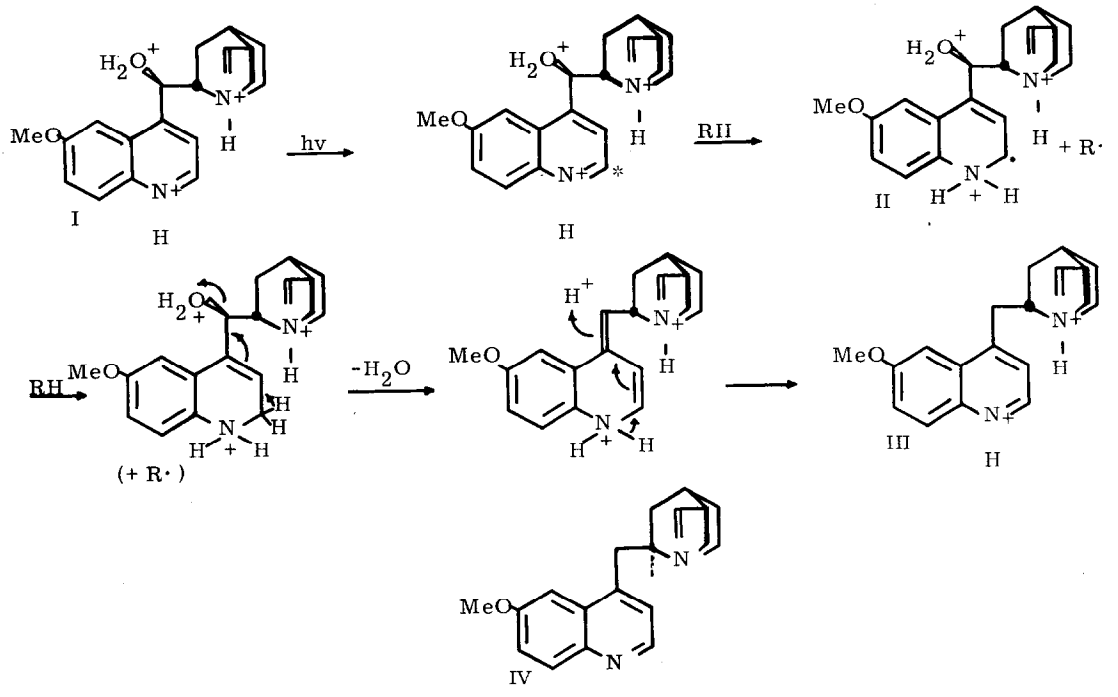
With the current interest in antimalarial agents, it was desirable to investigate reports of potential antimalarial compounds in ultraviolet irradiated aqueous acid solutions of quinine (1,2). The work of Kyker, McEwen, and Cornatzer, one of the last on the topic, merited detailed examination (2). Isomeric quinidine (2) has also been reported to be photochemically active.

Quinine (approximately 0.01 mole/700 ml) was irradiated through quartz with a 550-watt Hanovia lamp in 2N HCl solution, and the reaction progress was monitored by silica gel tlc. The reaction solution developed a product which migrated faster than the parent alkaloid. The irradiation was terminated after 70 hours at which time 40-50% of the quinine could be recovered. The solution was made alkaline, extracted, and separated via alumina column chromatography to provide a photoproduct in a 10% yield (% of starting material). Infrared, ultraviolet, elemental, and nmr analyses proved this compound to be deoxyquinine (the unprotonated form of III). The compound was synthesized by means of the known route (3) and compared to the photoproduct as a final proof of identity. The yield of III was increased to 32% and the reaction time reduced to a third when the irradiation was done in a 23:77 2-propanol: 2N HCl solution.

Quinidine undergoes an analogous reaction to provide deoxyquinidine (IV). This structure has also been proven by comparison to IV synthesized by the method of Heidelberger and Jacobs (4).

The remaining asymmetric centers of deoxyquinine and deoxyquinidine did not isomerize during the irradiation. Optical rotations of these compounds were identical with those of the respective independently synthesized compounds (3,4).

This reduction does not conform to any of the known photochemical oxidation-reduction reactions and is, therefore, a new photochemical reaction. The proposed mechanism of formation of III is illustrated below. The formation of II has been postulated as an intermediate



for the photoalkylation of the quinoline ring with alcohols (5, 6). Since the present reaction proceeds in the absence of alcohols, the alkylation pathway is not followed, and the alternate reduction route is taken. The formation of the intermediate radical II could also account for the dimeric photoproducts of quinoline and pyridine observed by Pfordte and Leuschner (7).

Evidence for the reduction mechanism is provided by several observations. The presence of a hydrogen atom donor, 2-propanol, enhanced the yield of III, the amount of III produced was maximized in relatively concentrated acid solutions, and the reaction proceeded with a pyrex filter. In dilute acid solutions a rapid reaction was observed to give mainly polymeric products. No degradation of the starting materials was observed with 2N HCl solutions of quinine and quinidine in the absence of ultraviolet light. The testing for antimalarial action by the photoproducts is in progress.

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