Hydrogen Isotope Exchange in Methyl-quinones

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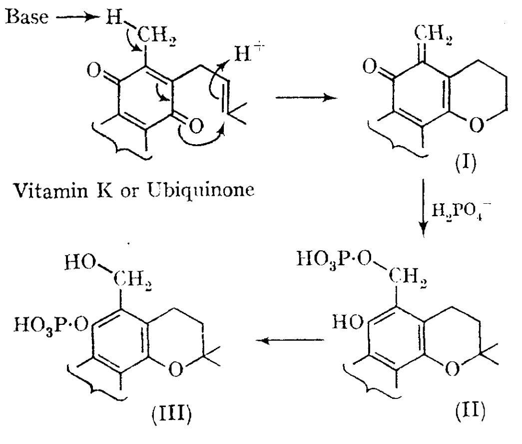
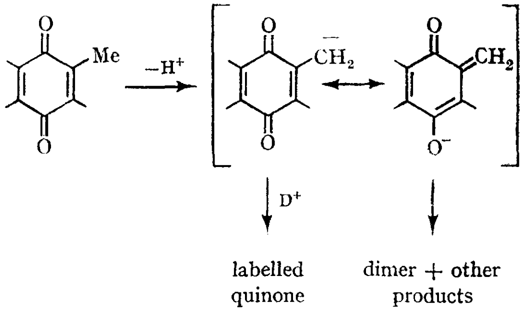
PHOSPHORYL TRANSFER accompanies the oxidation of hydroquinone phosphates.[1] This observation led to the suggestion[2] that the hydroquinone phosphates derived from vitamin K and ubiquinone might participate in the oxidative phosphorylation associated with electron transport in bacteria and mitochondria. Both these quinones contain a number of structural features in common,[3] particular attention having been paid to reactions involving the methyl group attached to the quinonoid nucleus. Vilkas and Lederer[2] proposed the intermediate formation of the quinone methide (I) leading, *via* the chromanyl phosphate (II), to (III). Isotopic evidence in support of the proton removal from methyl quinones, necessary for this scheme, has been singularly elusive, both *in vivo*[4] and *in vitro*.[5]



We now report the base-catalysed incorporation of both deuterium and tritium into methyl-quinones thereby providing evidence for intermediate anions of the quinone methide type:



Thus, duroquinone, recovered after having been heated under reflux for several hours in dioxan–D_2O with triethylamine, or potassium carbonate, was found to contain deuterium, the infrared spectrum containing bands attributable to C–D stretching at 2260, 2220, 2130 and 2060 cm.$^{-1}$.

Using tritiated water, it was possible to determine the degree of isotope incorporation. In a typical reaction using triethylamine and 2,3-dimethylnaphthaquinone, isotopic equilibrium (in which the recovered quinone contained the same proportion of tritium as did the water) was reached after 10 hr. under reflux in aqueous dioxan. Vitamin K was unstable under these conditions but tritium uptake into perhydro-vitamin K was readily observed.

Isotope incorporation is greatly dependent on the nature of the base, temperature, and apparent pH (*cf.* ref. 5). Moreover, both the rate and the products of reaction are extremely sensitive to change in the type of base. Using cyclic secondary amines, *e.g.*, piperidine,[6] or pyrrolidine no isotopically substituted methylquinone could be recovered. A fast and complex reaction involving the amine supervened. In the case of pyrrolidine and duroquinone, reaction was complete within a few minutes at room temperature; radical formation was indicated by a broad intense e.s.r. signal. This and other features are under further investigation.

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